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=> e tsoi j/au

E1            2     TSOI I N/AU
E2            1     TSOI IUA/AU
E3            0 --> TSOI J/AU
E4            4     TSOI K N/AU
E5            3     TSOI K V/AU
E6            1     TSOI K W/AU
E7            6     TSOI L A/AU
E8            1     TSOI L P/AU
E9            1     TSOI L S/AU
E10           2     TSOI M/AU
E11           8     TSOI M M/AU
E12          35     TSOI M S/AU

=> file biosis

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.90       1.05

FILE 'BIOSIS' ENTERED AT 11:16:26 ON 15 MAY 1997
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 12 May 1997 (970512/ED)
CAS REGISTRY NUMBERS (R) LAST ADDED: 12 May 1997 (970512/UP)


=> e tsoi j/au

E1            2     TSOI I M/AU
E2            2     TSOI I N/AU
E3            0 --> TSOI J/AU
E4            1     TSOI K C/AU
E5            4     TSOI K M/AU
E6            3     TSOI K N/AU
E7            2     TSOI K W/AU
E8            5     TSOI L A/AU
E9            1     TSOI L P/AU
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E11           2     TSOI M/AU
E12           9     TSOI M M/AU
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=> file medline, biosis

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.60       1.65

FILE 'MEDLINE' ENTERED AT 11:17:06 ON 15 MAY 1997

FILE 'BIOSIS' ENTERED AT 11:17:06 ON 15 MAY 1997
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=> e khosla c/au

E1            3      KHOSLA B/AU
E2           18      KHOSLA B K/AU
E3           81 --> KHOSLA C/AU
E4            9      KHOSLA D/AU
E5            7      KHOSLA H K/AU
E6            5      KHOSLA H L/AU
E7            1      KHOSLA H M/AU
E8            1      KHOSLA I N/AU
E9           16      KHOSLA J/AU
E10           1      KHOSLA J K/AU
E11           2      KHOSLA K/AU
E12          35      KHOSLA M/AU

=> s e3

L2           32 FILE MEDLINE
L3           49 FILE BIOSIS

TOTAL FOR ALL FILES
L4           81 "KHOSLA C"/AU

=> s l4 and py=1995


L5            4 FILE MEDLINE

L6            5 FILE BIOSIS

TOTAL FOR ALL FILES
L7            9 L4 AND PY=1995

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DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L7
L8 5 DUPLICATE REMOVE L7 (4 DUPLICATES REMOVED)

=> d 1-5 bib ab

L8 ANSWER 1 OF 5 MEDLINE DUPLICATE 1
AN 95362689 MEDLINE
TI Expression of a functional fungal polyketide synthase in the bacterium Streptomyces coelicolor A3(2).
AU Bedford D J; Schweizer E; Hopwood D A; ***Khosla C***
CS Department of Chemical Engineering, Stanford University, California 94305-5025, USA..
SO JOURNAL OF BACTERIOLOGY, ***(1995 Aug)*** 177 (15) 4544-8. Journal code: HH3. ISSN: 0021-9193.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9511
AB The multifunctional 6-methylsalicylic acid synthase gene from Penicillium patulum was engineered for regulated expression in Streptomyces coelicolor. Production of significant amounts of 6-methylsalicylic acid by the recombinant strain was proven by nuclear magnetic resonance spectroscopy. These results suggest that it is possible to harness the molecular diversity of eukaryotic polyketide pathways by heterologous expression of biosynthetic genes in an easily manipulated model bacterial host in which prokaryotic aromatic and modular polyketide synthase genes are already expressed and recombined.

L8 ANSWER 2 OF 5 MEDLINE DUPLICATE 2
AN 95378087 MEDLINE
TI Erythromycin biosynthesis. Highly efficient incorporation of polyketide chain elongation intermediates into 6-deoxyerythronolide B in an engineered Streptomyces host.
AU Cane D E; Luo G; ***Khosla C*** ; Kao C M; Katz L
CS Department of Chemistry, Brown University, Providence, Rhode Island 02912, USA..
NC GM22172 (NIGMS)
SO JOURNAL OF ANTIBIOTICS, ***(1995 Jul)*** 48 (7) 647-51. Journal code: HCF. ISSN: 0021-8820.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals; Cancer Journals
EM 9512
AB Feeding of (2S,3R)-[2,3-13C2]-2-methyl-3-hydroxypentanoyl NAC thioester (1a) to the recombinant organism Streptomyces coelicolor CH999/pCK7 harboring the complete set of eryA genes from Saccharopolyspora erythraea encoding the 6-deoxyerythronolide B synthase (DEBS) resulted in the formation of 6-deoxyerythronolide B (2a) labeled with 13C at C-12 and C-13, as evidenced by the appearance of a pair of enhanced and coupled doublets in the 13C NMR spectrum. The level of 13C enrichment was 15-20 atom% 13C, as much as 100 times higher than the usually observed efficiency of incorporation of NAC thioesters into polyketide metabolites. Similar incorporation of (2S,3R)-[3-2H,3-13C]-2-methyl-3-hydroxypentanoyl NAC thioester (1b) gave 6-deoxyerythronolide B (2b) labeled with both 13C and deuterium at C-13. The intact incorporation of both precursors confirms the normal functioning of the recombinant DEBS proteins in the heterologous host.

L8 ANSWER 3 OF 5 MEDLINE DUPLICATE 3
AN 95312073 MEDLINE
TI Rational design of aromatic polyketide natural products by recombinant assembly of enzymatic subunits [see comments].
CM Comment in: Nature 1995 Jun 15;375(6532):533
AU McDaniel R; Ebert-Khosla S; Hopwood D A; ***Khosla C***
CS Department of Chemical Engineering, Stanford University, California 94305-5025, USA.
SO NATURE, ***(1995 Jun 15)*** 375 (6532) 549-54.
Journal code: NSC. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9509
AB Recent advances in understanding of bacterial aromatic polyketide biosynthesis allow the development of a set of design rules for the rational manipulation of chain synthesis, reduction of keto groups and early cyclization steps by genetic engineering. The concept of rational design is illustrated by the preparation of Streptomyces strains that produce two new polyketides by expression of combinations of appropriate enzymatic subunits from naturally occurring polyketide synthases. The potential for generating molecular diversity within this class of molecules by genetic engineering is enormous.

L8 ANSWER 4 OF 5 MEDLINE DUPLICATE 4
AN 96069758 MEDLINE

TI Cell-free synthesis of polyketides by recombinant erythromycin polyketide synthases.
AU Pieper R; Luo G; Cane D E; ***Khosla C***
CS Department of Chemical Engineering, Stanford University, California 94305-5025, USA..
SO NATURE, ***(1995 Nov 16)*** 378 (6554) 263-6.
Journal code: NSC. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9602
AB Modular polyketide synthases (PKSs) are complex multi-enzyme proteins that catalyse the bacterial biosynthesis of many pharmaceutically useful polyketides. The PKSs are organized into a series of modules, each containing the active catalytic sites required for one step in the synthesis process. Here we report a method for cell-free enzymatic synthesis of 6-deoxyerythronolide B (6-dEB), the parent molecule of the antibiotic erythromycin A, using recombinant 6-deoxyerythronolide B synthase (DEBS), a modular PKS with at least 28 distinct active sites. We have also synthesized in vitro a triketide lactone by using a truncated mutant of DEBS. The availability of such cell-free synthetic routes will allow direct investigation of the structural and mechanistic basis for the unusual combination of high substrate specificity and tolerance to genetic reprogramming found in this enzyme family.

L8 ANSWER 5 OF 5 BIOSIS COPYRIGHT 1997 BIOSIS
AN 95:239974 BIOSIS
DN 98254274
TI Engineering biosynthesis of "unnatural" natural products.
AU ***Khosla C***
CS Dep. Chem. Eng., Stanford Univ., Stanford, CA 94305-5025, USA
SO 209th American Chemical Society National Meeting, Anaheim, California, USA, April 2-6, 1995. Abstracts of Papers American Chemical Society 209 (1-2). 1995. MEDI 233. ISSN: 0065-7727
DT Conference
LA English

=> d his

(FILE 'HOME' ENTERED AT 11:14:27 ON 15 MAY 1997)

FILE 'MEDLINE' ENTERED AT 11:14:41 ON 15 MAY 1997
E KHOSLA/AU
L1 32 S E11

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                E TSOI J/AU

      FILE 'BIOSIS' ENTERED AT 11:16:26 ON 15 MAY 1997
                E TSOI J/AU

      FILE 'MEDLINE, BIOSIS' ENTERED AT 11:17:06 ON 15 MAY 1997
                E KHOSLA C/AU
L2             32 FILE MEDLINE
L3             49 FILE BIOSIS
      TOTAL FOR ALL FILES
L4             81 S E3
L5              4 FILE MEDLINE
L6              5 FILE BIOSIS
      TOTAL FOR ALL FILES
L7              9 S L4 AND PY=1995
L8              5 DUPLICATE REMOVE L7 (4 DUPLICATES REMOVED)

=> s l4 and py=1994

L9              4 FILE MEDLINE
L10             9 FILE BIOSIS

TOTAL FOR ALL FILES
L11            13 L4 AND PY=1994

=> duplicate remove l11

DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n

PROCESSING COMPLETED FOR L11
L12            10 DUPLICATE REMOVE L11 (3 DUPLICATES REMOVED)

=> d 1-10 bib ab


L12  ANSWER 1 OF 10  BIOSIS  COPYRIGHT 1997 BIOSIS
AN  95:106380  BIOSIS
DN  98120680
TI  Engineered Biosynthesis of a Triketide Lactone form an Incomplete
    Modular Polyketide Synthase.
AU  Kao C M; Luo G; Katz L; Cane D E;   ***Khosla C***
CS  Dep. Chem. Eng., Stanford Univ., Stanford, CA 94305-5025, USA
SO  Journal of the American Chemical Society 116 (25). 1994.
    11612-11613. ISSN: 0002-7863
LA  English
```

L12 ANSWER 2 OF 10 MEDLINE DUPLICATE 1
AN 95062304 MEDLINE
TI Engineered biosynthesis of novel polyketides: influence of a downstream enzyme on the catalytic specificity of a minimal aromatic polyketide synthase.
AU McDaniel R; Ebert-Khosla S; Fu H; Hopwood D A; ***Khosla C***
CS Department of Chemical Engineering, Stanford University, CA 94305-5025..
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, ***(1994 Nov 22)*** 91 (24) 11542-6.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9502
AB To identify the minimum set of polyketide synthase (PKS) components required for in vivo biosynthesis of aromatic polyketides, combinations of genes encoding subunits of three different aromatic PKSs--act from Streptomyces coelicolor A3(2) (an actinorhodin producer), fren from Streptomyces roseofulvus (a frenolicin and nanaomycin producer), and tcm from Streptomyces glaucescens (a tetracenomycin producer)--were expressed in a recently developed Streptomyces host-vector system. The "minimal" components (ketosynthase/putative acyltransferase, chain length-determining factor, and acyl carrier protein) were produced with and without a functional polyketide ketoreductase and/or cyclase, and the polyketide products of these recombinant strains were structurally characterized. Several previously identified polyketides were isolated in addition to two previously unidentified polyketides, dehydromutactin and SEK 15b, described here. The results proved that the act cyclase is not required for the biosynthesis of several aberrantly cyclized products that have been previously reported. They are also consistent with earlier conclusions that the minimal PKS controls chain length as well as the regiospecificity of the first cyclization and that it can do so in the absence of both a ketoreductase and a cyclase. However, the ability of the minimal tcm PKS to synthesize two different singly cyclized intermediates suggests that it is unable to accurately control the course of this reaction by itself. In the presence of a downstream enzyme, the flux through one branch of the cyclization pathway increases relative to the other. We propose that these alternative specificities may be due to the ability of downstream enzymes to associate with the minimal PKS and to selectively inhibit a particular branch of the cyclization pathway.

L12 ANSWER 3 OF 10 BIOSIS COPYRIGHT 1997 BIOSIS

AN 95:76990 BIOSIS
DN 98091290
TI Engineered biosynthesis of novel polyketides: actVII and actIV genes encode aromatase and cyclase enzymes, respectively.
AU McDaniel R; Ebert-Khosla S; Hopwood D A; ***Khosla C***
CS Dep. Chem. Eng., Stanford Univ., Stanford, CA 94305-5025, USA
SO Journal of the American Chemical Society 116 (24). 1994. 10855-10859. ISSN: 0002-7863
LA English

L12 ANSWER 4 OF 10 MEDLINE DUPLICATE 2
AN 94325299 MEDLINE
TI Engineered biosynthesis of novel polyketides: stereochemical course of two reactions catalyzed by a polyketide synthase.
AU Fu H; McDaniel R; Hopwood D A; ***Khosla C***
CS Department of Chemical Engineering, Stanford University, California 94305-5025.
SO BIOCHEMISTRY, ***(1994 Aug 9)*** 33 (31) 9321-6.
Journal code: A0G. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9411
AB A genetically engineered strain expressing the essential components of the tetracenomycin polyketide synthase (tcm PKS) along with the actinorhodin ketoreductase (act KR) was found to produce two new (diastereomeric) aromatic polyketides, designated RM20b and RM20c, in addition to RM20, whose structure was reported earlier [McDaniel, R., Ebert-Khosla, S., Hopwood, D. A., & Khosla, C. (1993) Science 262, 1546-1550]. Spectroscopic and in vivo isotopic labeling analysis of RM20b and RM20c revealed that their polyketide backbones were identical to that of RM20 with respect to chain length, regiospecificity of ketoreduction, and regiospecificity of the first intramolecular aldol condensation. This is consistent with earlier predictions that the essential components of the PKS--a bifunctional ketosynthase/acyltransferase, a chain length determining factor, and an acyl carrier protein--are responsible for controlling each of these features of the polyketide backbone [McDaniel, R., Ebert-Khosla, S., Hopwood, D. A., & Khosla, C. (1993) Science 262, 1546-1550; McDaniel, R., Ebert-Khosla, S., Hopwood, D. A., & Khosla, C. (1993) J. Am. Chem. Soc. 115, 11671-11675; Fu, H., Ebert-Khosla, S., Hopwood, D. A., & Khosla, C. (1994) J. Am. Chem. Soc. 116, 4166-4170]. In addition, however, RM20b and RM20c possess two unusual features. In both molecules the hydroxyls on sp3 C-9 and C-7 of the first six-membered ring, which arise as a result of ketoreduction and aldol condensation, respectively, are intact,

rather than being lost via dehydration. Furthermore, the relative yield of RM20b (in which these hydroxyls are syn) is 7-fold greater than that of RM20c (in which they are anti).(ABSTRACT TRUNCATED AT 250 WORDS)

L12 ANSWER 5 OF 10 BIOSIS COPYRIGHT 1997 BIOSIS
AN 94:404114 BIOSIS
DN 97417114
TI Relaxed specificity of the oxytetracycline polyketide synthase for an acetate primer in the absence of a malonamyl primer.
AU Fu H; Ebert-Khosla S; Hopwood D A; ***Khosla C***
CS Dep. Chem. Eng., Stanford Univ., Stanford, CA 94305-5025, USA
SO Journal of the American Chemical Society 116 (14). 1994. 6443-6444. ISSN: 0002-7863
LA English

L12 ANSWER 6 OF 10 BIOSIS COPYRIGHT 1997 BIOSIS
AN 94:314068 BIOSIS
DN 97327068
TI Engineered biosynthesis of novel polyketides: Dissection of the catalytic specificity of the act ketoreductase.
AU Fu H; Ebert-Khosla S; Hopwood D A; ***Khosla C***
CS Dep. Chemical Eng., Stanford University, Stanford, CA 94305-5025, USA
SO Journal of the American Chemical Society 116 (10). 1994. 4166-4170. ISSN: 0002-7863
LA English

L12 ANSWER 7 OF 10 MEDLINE
AN 94235217 MEDLINE
TI Efficient sampling of protein sequence space for multiple mutants.
AU Caren R; Morkeberg R; ***Khosla C***
CS Department of Chemical Engineering, Stanford University, CA 94305-5025..
SO BIO/TECHNOLOGY, ***(1994 May)*** 12 (5) 517-20. Journal code: AL1. ISSN: 0733-222X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS B
EM 9408
AB We describe here a method capable of generating a very large population of multiple mutants, the size of which is primarily limited by volume constraints. This method, referred to as recombination-enhanced mutagenesis, combines the power of in vitro mutagenesis with the high frequencies of in vivo recombination that can be achieved using single-stranded transduction systems. The recombination frequency between two mutations separated by as little

as 19 amino acids is 0.02; this frequency approaches a value of 0.1 for mutations separated by more than 38 amino acids. Up to 10(8) independent recombinants were generated in 1 ml of an E. coli culture, and this number scales linearly (or better) with increasing volume. To prove the method's effectiveness, we applied it to the problem of reverting multiple mutants of mouse dihydrofolate reductase, which could not be reverted using mutagenesis alone. Thus, given an appropriate screen or selection scheme, recombination-enhanced mutagenesis is well-suited for addressing a range of combinatorially complex problems, such as antigen recognition, enzyme catalysis, protein folding, and transport/transduction across biomembranes.

L12 ANSWER 8 OF 10 MEDLINE DUPLICATE 3
AN 94310433 MEDLINE
TI Engineered biosynthesis of a complete macrolactone in a heterologous host.
AU Kao C M; Katz L; ***Khosla C***
CS Department of Chemical Engineering, Stanford University, CA 94305-5025.
SO SCIENCE, ***(1994 Jul 22)*** 265 (5171) 509-12.
Journal code: UJ7. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9410
AB Macrocyclic polyketides have been subjects of great interest in synthetic and biosynthetic chemistry because of their structural complexity and medicinal activities. With expression of the entire 6-deoxyerythronolide B synthase (DEBS) (10,283 amino acids) in a heterologous host, substantial quantities of 6-deoxyerythronolide B (6dEB), the aglycone of the macrolide antibiotic erythromycin, and 8,8a-deoxyoleandolide, a 14-membered lactone ring identical to 6dEB except for a methyl group side chain in place of an ethyl unit, were synthesized in Streptomyces coelicolor. The biosynthetic strategy utilizes a genetic approach that facilitates rapid structural manipulation of DEBS or other modular polyketide synthases (PKSs), including those found in actinomycetes with poorly developed genetic methods. From a technological viewpoint, this approach should allow the rational design of biosynthetic products and may eventually lead to the generation of diverse polyketide libraries by means of combinatorial cloning of naturally occurring and mutant PKS modules.

L12 ANSWER 9 OF 10 BIOSIS COPYRIGHT 1997 BIOSIS
AN 94:193043 BIOSIS
DN 97206043

TI Engineered biosynthesis of novel polyketides.
AU McDaniel R; Ebert-Khosla S; ***Khosla C***
CS Dep. Chem. Eng., Stanford Univ., Stanford, CA 94305-5025, USA
SO 207th National Meeting of the American Chemical Society, San Diego, California, USA, March 13-17, 1994. Abstracts of Papers American Chemical Society 207 (1-2). 1994. BIOT 221. ISSN: 0065-7727
DT Conference
LA English

L12 ANSWER 10 OF 10 BIOSIS COPYRIGHT 1997 BIOSIS
AN 94:193762 BIOSIS
DN 97206762
TI Study of aromatic polyketide synthases using a Streptomyces host-vector system.
AU Fu H; McDaniel R; Ebert-Khosla S; ***Khosla C***
CS Dep. Chem. Engineering, Stanford Univ., Stanford, CA 94305-5025, USA
SO 207th National Meeting of the American Chemical Society, San Diego, California, USA, March 13-17, 1994. Abstracts of Papers American Chemical Society 207 (1-2). 1994. ORGN 18. ISSN: 0065-7727
DT Conference
LA English

=> s combinatorial and (gene or library)

L13 747 FILE MEDLINE
L14 874 FILE BIOSIS

TOTAL FOR ALL FILES
L15 1621 COMBINATORIAL AND (GENE OR LIBRARY)

=> s l15 and species

L16 47 FILE MEDLINE
L17 37 FILE BIOSIS

TOTAL FOR ALL FILES
L18 84 L15 AND SPECIES

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DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L18
L19 56 DUPLICATE REMOVE L18 (28 DUPLICATES REMOVED)

=> d 1-56 bib ab

L19 ANSWER 1 OF 56 MEDLINE DUPLICATE 1
AN 96210038 MEDLINE
TI Construction of a ***combinatorial*** IgE ***library*** from an allergic patient. Isolation and characterization of human IgE Fabs with specificity for the major timothy grass pollen allergen, Phl p 5.
AU Steinberger P; Kraft D; Valenta R
CS Institute of General and Experimental Pathology, AKH, University of Vienna, Austria.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 May 3) 271 (18) 10967-72. Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-X95746; GENBANK-X95747; GENBANK-X95748; GENBANK-X95749; GENBANK-X95750
EM 9609
AB To characterize human IgE antibodies with specificity for a major allergen at the molecular level, we have constructed an IgE ***combinatorial*** ***library*** from a grass pollen allergic patient. cDNAs coding for IgE heavy chain fragments and for light chains were reverse-transcribed and polymerase chain reaction-amplified from RNA of peripheral blood lymphocytes and randomly combined in plasmid pComb3H to yield a ***combinatorial*** ***library*** of 5 x 10(7) primary clones. IgE Fabs with specificity for Phl p 5, a major timothy grass pollen allergen, were isolated by panning. Sequence analysis showed that the 4 of the Fabs used the same heavy chain fragments which had combined with different kappa light chains. Soluble recombinant IgE Fabs were purified by affinity chromatography to Phl p 5 and, like natural IgE antibodies, cross-reacted with group 5 allergens from different grass ***species*** . The described approach should facilitate studies on the molecular interaction between IgE antibodies and allergens and encourages the consideration of specific IgE Fabs that are capable of interfering with allergen-IgE binding as potential therapeutic tools.

L19 ANSWER 2 OF 56 MEDLINE DUPLICATE 2
AN 96180200 MEDLINE
TI Extensive diversity of transcribed TCR-beta in phylogenetically primitive vertebrate.
AU Hawke N A; Rast J P; Litman G W
CS Department of Medical Microbiology and Immunology, University of South Florida, Tampa 33612, USA.

SO JOURNAL OF IMMUNOLOGY, (1996 Apr 1) 156 (7) 2458-64.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9611
AB The genetic complexity of the expressed TCR Vbeta repertoire in Heterodontus francisci, the horned shark, a member of the most phylogenetically primitive vertebrate class in which TCR ***genes*** have been identified, is addressed. The sequences of 55 spleen cDNA clones encoding TCR-beta ***genes*** are compared, and 7 diverse Vbeta families are defined by overall sequence identity and clustering based on phylogenetic distance analyses. At least 18 putative Jbeta sequence types, as well as a consensus diversity (D) element that resembles most closely mammalian TCR Dbeta, can he recognized. Extensive sequence diversity, as well as characteristic TCR-beta length variation in CDR3, is evident. Unlike Ig ***genes*** in this ***species*** , TCR-beta ***genes*** exhibit considerable V family multiplicity and appear to utilize ***combinatorial*** mechanisms in the generation of immunologic diversity. in this sense, the TCR-beta ***genes*** in this cartilaginous fish and humans are more similar than are the ***genes*** encoding Ab proteins in these ***species*** .

L19 ANSWER 3 OF 56 MEDLINE DUPLICATE 3
AN 96286075 MEDLINE
TI Cloning and analysis of IgG kappa and IgG lambda anti-thyroglobulin autoantibodies from a patient with Hashimoto's thyroiditis: evidence for in vivo antigen-driven repertoire selection.
AU McIntosh R S; Asghar M S; Watson P F; Kemp E H; Weetman A P
CS Department of Medicine, University of Sheffield Clinical Sciences Center, Northern General Hospital, United Kingdom.
SO JOURNAL OF IMMUNOLOGY, (1996 Jul 15) 157 (2) 927-35.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
OS GENBANK-X92990; GENBANK-X92991; GENBANK-X92992; GENBANK-X92993; GENBANK-X92994; GENBANK-X92995; GENBANK-X92996; GENBANK-X92997; GENBANK-X92998; GENBANK-X92999; GENBANK-X93000; GENBANK-X93001; GENBANK-X93002; GENBANK-X93003; GENBANK-X93004; GENBANK-X93005; GENBANK-X93006; GENBANK-X93007; GENBANK-X93008
EM 9701
EW 19970104

AB Antibodies to thyroglobulin (Tg) are commonly found in patients with the autoimmune thyroid diseases Graves' disease and Hashimoto's thyroiditis as well as in individuals with apparently normal thyroid function. Although it is not clear how Tg Abs are involved in the pathology of the diseases, the study and analysis of these Abs may nevertheless be instructive in allowing the development of an Ab response to an autoimmune disease-associated self Ag to be followed. We have prepared IgG kappa and lambda phage display ***combinatorial*** ***libraries*** from the cervical lymph node of a single Hashimoto's thyroiditis patient with a high anti-Tg titer. These were selected with purified human Tg, and 10 IgG kappa and 9 IgG lambda clones were analyzed further. Sequence analysis of the clones showed a very highly restricted heavy chain usage and a less restricted light chain usage. There was a variable degree of divergence from germ-line sequence in the light chain sequences, with a clear relationship between relatively higher affinity of the Fab for human Tg and an increased degree of somatic hypermutation. The Tg-selected Fab did not bind to Tg from other ***species*** , to reduced denatured Tg, or to thyroid peroxidase. The Fab inhibited patient serum binding to human Tg by between 39 and 79%. In summary, we have isolated 19 high affinity, human Tg-specific Fab and shown that the relative affinity of the Fab is directly related to the pattern of somatic hypermutation.

L19 ANSWER 4 OF 56 MEDLINE
AN 96415274 MEDLINE
TI Synthesis of five enantiomerically pure haptens designed for in vitro evolution of antibodies with peptidase activity.
AU Wagner J; Lerner R A; Barbas C F 3rd
CS Department of Chemistry and Molecular Biology, Scripps Research Institute, La Jolla, CA 92037, USA.
NC PO CA27489 (NCI)
SO BIOORGANIC AND MEDICINAL CHEMISTRY, (1996 Jun) 4 (6) 901-16. Journal code: B38. ISSN: 0968-0896.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9704
EW 19970403
AB A series of five haptens have been synthesized for use in vitro selection experiments from ***combinatorial*** antibody ***libraries*** . Haptens were designed for the recruitment of serine and cysteine protease reaction mechanisms for the cleavage of Phe-Ala and Phe-Phe (L,L) dipeptide analogues. For the selection of transition state stabilization, PheP(O)Ala (7) and PheP(O)Phe (10) derivatives were synthesized using the Mitsunobu approach where

hybridization.

US PAT NO: 5,641,869 :IMAGE AVAILABLE: L2: 8 of 36

DETDESC:

DETD(53)

Libraries are screened with probes or analytical tools designed to identify the gene of interest or the protein encoded by it. For cDNA expression **libraries**, suitable probes include monoclonal or polyclonal antibodies that recognize and specifically bind to HRG; oligonucleotides of about 20-80 bases in length that encode known or suspected portions of HRG cDNA from the **same** or **different species**; and/or complementary or homologous cDNAs or fragments thereof that encode the **same** or a hydridizing gene. Appropriate probes for screening genomic DNA **libraries** include, but are not limited to, oligonucleotides; cDNAs or fragments thereof that encode the **same** or hybridizing DNA; and/or homologous genomic DNAs or fragments thereof. Screening the cDNA or genomic **library** with the selected probe may be conducted using standard procedures as described in chapters 10-12 of Sambrook et al., supra.

US PAT NO: 5,639,949 :IMAGE AVAILABLE: L2: 9 of 36

DETDESC:

DETD(27)

Genes . . . maintains the APS-conferring ability further characterized. Whereas the host organism lacking the ability to produce the APS may be a **different species** to the organism from which the APS derives, a variation of this technique involves the transformation of host DNA into the **same** host which has had its APS-producing ability disrupted by mutagenesis. In this method, an APS-producing organism is mutated and non-APS. . . . of their sequence homology to the biosynthetic genes of the known compounds. Techniques suitable for cloning by homology include standard **library** screening by DNA hybridization.

US PAT NO: 5,635,601 :IMAGE AVAILABLE: L2: 10 of 36

DETDESC:

DETD(30)

The DNA encoding the beta-8 integrin subunit may be obtained from any cDNA **library** prepared from tissue believed to possess the beta-8 integrin subunit mRNA and to express it at a detectable level. The beta-8 integrin subunit gene may also be obtained from a genomic **library**. **Libraries** are screened with probes designed to identify the gene of interest or the protein encoded by it. For cDNA expression **libraries**, suitable probes include monoclonal or polyclonal antibodies that recognize and specifically bind to the beta-8 integrin subunit; oligonucleotides of about 20-80 bases in length that encode known or suspected portions of the beta-8 integrin subunit cDNA from the **same** or **different species**; and/or complementary or homologous cDNAs or fragments thereof that encode the **same** or a similar gene. Appropriate probes for screening genomic DNA **libraries** include, but are not limited to, oligonucleotides; cDNAs or fragments thereof that encode the **same** or a similar gene; and/or homologous genomic DNAs or fragments thereof. Screening the cDNA or genomic **library** with the selected probe may be conducted using standard procedures as described in chapters 10-12 of Sambrook et al., supra.

=> d 11-36 kwic

US PAT NO: 5,627,075 :IMAGE AVAILABLE: L2: 11 of 36

DETDESC:

DETD(78)

Libraries are screened with probes designed to identify the gene of interest or the protein encoded by it. For cDNA expression **libraries**, suitable probes include, e.g.: monoclonal or polyclonal antibodies that recognize and specifically bind to the CHF; oligonucleotides of about 20-80 bases in length that encode known or suspected portions of the CHF cDNA from the **same** or **different species**; and/or complementary or homologous cDNAs or fragments thereof that encode the **same** or a similar gene. Appropriate probes for screening genomic DNA **libraries** include, but are not limited to, oligonucleotides, cDNAs, or fragments thereof that encode the **same** or a similar gene, and/or homologous genomic DNAs or fragments thereof. Screening the cDNA or genomic **library** with the selected probe may be conducted using standard procedures as described in chapters 10-12 of Sambrook et al., supra.

US PAT NO: 5,624,806 :IMAGE AVAILABLE: L2: 12 of 36

DETDESC:

DETD(79)

Libraries are screened with probes designed to identify the gene of interest or the protein encoded by it. For cDNA expression **libraries**, suitable probes include, e.g.: monoclonal or polyclonal antibodies that recognize and specifically bind to the CHF; oligonucleotides of about 20-80 bases in length that encode known or suspected portions of the CHF cDNA from the **same** or **different species**; and/or complementary or homologous cDNAs or fragments thereof that encode the **same** or a similar gene. Appropriate probes for screening genomic DNA **libraries** include, but are not limited to, oligonucleotides, cDNAs, or fragments thereof that encode the **same** or a similar gene, and/or homologous genomic DNAs or fragments thereof. Screening the cDNA or genomic **library** with the selected probe may be conducted using standard procedures as described in chapters 10-12 of Sambrook et al.. supra.

US PAT NO: 5,614,194 :IMAGE AVAILABLE: L2: 13 of 36

DETDESC:

DETD(8)

The . . . be detected by hybridization using the originally cloned. cDNA as a probe. Clones derived either from cDNA or genomic DNA **libraries** could be identified in this manner, based upon the homology between DNA segments coding for the sporozoite antigen of **different** Plasmodium **species**. Identification of clones expressing an immunoreactive protein was done by screening lysates of colonies of cells transformed (as above) with the cloned cDNA. **Pools** of 48 colonies were screened using a sensitive, two-site immunoradiometric assay performed with monoclonal antibodies. This permitted the detection of. . .

US PAT NO: 5,612,471 :IMAGE AVAILABLE: L2: 14 of 36

DETDESC:

DETD(10)

Other . . . sequences of previously identified nematode-induced genes can be used to isolate the desired gene in a cDNA or genomic DNA **library**. These techniques can be used to isolate homologous genes in the **same** or **different** plant **species**. The use of such hybridization techniques for identifying homologous genes is well known in the art and need not be. . .

US PAT NO: 5,608,145 :IMAGE AVAILABLE: L2: 15 of 36

DETDESC:

DETD(7)

The cDNA or genomic **library** can then be screened using a probe based upon the sequence of a cloned gene such as that shown in. . . No. 1. Probes may be used to hybridize with genomic DNA or cDNA sequences to isolate homologous genes in the **same** or **different** plant **species**. The use of such hybridization techniques for identifying homologous genes is well known in the art and need not be. . .

US PAT NO: 5,571,893 :IMAGE AVAILABLE: L2: 16 of 36

DETDESC:

DETD(79)

Libraries are screened with probes designed to identify the gene of interest or the protein encoded by it. For cDNA expression **libraries**, suitable probes include, e.g.: monoclonal or polyclonal antibodies that recognize and specifically bind to the CHF; oligonucleotides of about 20-80 bases in length that encode known or suspected portions of the CHF cDNA from the **same** or **different species**; and/or complementary or homologous cDNAs or fragments thereof that encode the **same** or a similar gene. Appropriate probes for screening genomic DNA **libraries** include, but are not limited to, oligonucleotides, cDNAs, or fragments thereof that encode the **same** or a similar gene, and/or homologous genomic DNAs or fragments thereof. Screening the cDNA or genomic **library** with the selected probe may be conducted using standard procedures as described in chapters 10-12 of Sambrook et al.. supra.

US PAT NO: 5,571,675 :IMAGE AVAILABLE: L2: 17 of 36

DETDESC:

DETD(79)

Libraries are screened with probes designed to identify the gene of interest or the protein encoded by it. For cDNA expression **libraries**, suitable probes include, e.g.: monoclonal or polyclonal antibodies that recognize and specifically bind to the CHF; oligonucleotides of about 20-80 bases in length that encode known or suspected portions of the CHF cDNA from the **same** or **different species**; and/or complementary or homologous cDNAs or fragments thereof that encode the **same** or a similar gene. Appropriate probes for screening genomic DNA **libraries** include, but are not limited to, oligonucleotides, cDNAs, or fragments thereof that encode the **same** or a similar gene, and/or homologous genomic DNAs or fragments thereof. Screening the cDNA or genomic **library** with the selected probe may be conducted using standard procedures as described in chapters 10-12 of Sambrook et al. supra.

US PAT NO: 5,569,830 :IMAGE AVAILABLE: L2: 18 of 36

DETDESC:

DETD(11)

The cDNA or genomic l[redacted]ary can then be screened using [redacted]probe based upon the sequence of a cloned PGIP gene such as pear PGIP. . . . be used. Probes may be used to hybridize with genomic DNA or cDNA sequences to isolate homologous genes in the **same** or **different** plant **species**. The use of such hybridization techniques for identifying homologous genes is well known in the an and need not be. . .

US PAT NO: 5,534,660 :IMAGE AVAILABLE: L2: 19 of 36

DETDESC:

DETD(20)

The cDNA or genomic **library** can then be screened using a probe based upon the sequence of a cloned Ph gene such as Ph6. Probes may be used to hybridize with genomic DNA or cDNA sequences to isolate homologous genes in the **same** or **different** plant **species**. The use of such hybridization techniques for identifying homologous genes is well known in the art and need not be. . .

US PAT NO: 5,534,615 :IMAGE AVAILABLE: L2: 20 of 36

DETDESC:

DETD(76)

Libraries are screened with probes designed to identify the gene of interest or the protein encoded by it. For cDNA expression **libraries**, suitable probes include monoclonal or polyclonal antibodies that recognize and specifically bind to the CHF; oligonucleotides of about 20-80 bases in length that encode known or suspected portions of the CHF cDNA from the **same** or **different species**; and/or complementary or homologous cDNAs or fragments thereof that encode the **same** or a similar gene. Appropriate probes for screening genomic DNA **libraries** include, but are not limited to, oligonucleotides, cDNAs, or fragments thereof that encode the **same** or a similar gene, and/or homologous genomic DNAs or fragments thereof. Screening the cDNA or genomic **library** with the selected probe may be conducted using standard procedures as described in chapters 10-12 of Sambrook et al. supra.

US PAT NO: 5,504,197 :IMAGE AVAILABLE: L2: 21 of 36

DETDESC:

DETD(19)

Because mitogenic proteins from **different** mammalian **species** usually show high homologies, i.e., porcine, human, bovine, ovine and rat, such homologous mitogens from other species can be deduced using the **same** probes as were employed in searching the rat cDNA **libraries**. Alternatively, cDNA fragments of the gene sequence coding for the rat mitogen (or the entire sequence) can be used to probe the cDNA **library** of another species, e.g., human (see Example 1). Thus, the knowledge of the sequence of the rat mitogen allows the. . .

US PAT NO: 5,500,356 :IMAGE AVAILABLE: L2: 22 of 36

DETDESC:

DETD(2)

The present invention concerns an improved method for rapidly isolating a "desired" nucleic acid "clone" from a mixture or **library** of cloned molecules. The "clones" of the present invention comprise circular or

linear DNA or RNA molecules that may be either single-stranded or double-stranded. Typically, such clones or **libraries** will comprise plasmids or other vectors (such as viral vectors) that have been engineered to contain a fragment of DNA. . . or RNA derived from a source such as a homogeneous specimen (such as cells in tissue culture, cells of the **same** tissue, etc.), or a heterogeneous specimen (such as a mixture of pathogen-free and pathogen-infected cells, a mixture of cells of **different** tissues, **species**, or cells of the **same** or different tissue at different temporal or developmental stages, etc.). The cells, if any, of these nucleic acid sources may. . .

US PAT NO: 5,484,891 :IMAGE AVAILABLE: L2: 23 of 36

DETDESC:

DETD(61)

Libraries are screened with probes designed to identify the gene of interest or the protein encoded by it. For cDNA expression **libraries**, suitable probes usually include mono- and polyclonal antibodies that recognize and specifically bind to the desired protein; oligonucleotides of about 20-80 bases in length that encode known or suspected portions of the selectin ligand cDNA from the **same** or **different species**; and/or complementary or homologous cDNAs or their fragments that encode the **same** or similar gene.

US PAT NO: 5,408,041 :IMAGE AVAILABLE: L2: 24 of 36

DETDESC:

DETD(159)

The deer antler tip cDNA **library** fractions are screened by polymerase chain reaction (PCR) (Saiki, et al. (1988) Science 239: 487-491) for detection of deer IGF-I. . . previously been cloned, the oligonucleotides used for amplifying IGF sequences are designed from IGF-I and IGF-II regions highly conserved among **different species**. Specific IGF-I and IGF-II reactions are carried out separately. The IGF-I reactions utilize a sense-strand IGF-I specific oligonucleotide (with the. . . IGF-II sequences. The IGF-II reactions utilize a sense-strand IGF-II-specific primer (with the sequence 5'-ATGGGGATCCCAGTGGGGAAGTCGAT-3', :SEQ ID NO: 16:) and the **same** general downstream anti-sense IGF primer used for the IGF-I reactions. The sense primers has an engineered BamHI site and the. . . Electrophoresed, amplified DNA products of the expected size (.about. 150 bp) are obtained from IGF-I reactions from several of the **library** fractions. A single reaction, fraction 11, produces an IGF-II-specific product (.about.200 bp). The IGF-I and IGF-II PCR products are specifically. . .

US PAT NO: 5,367,060 :IMAGE AVAILABLE: L2: 25 of 36

DETDESC:

DETD(48)

Libraries are screened with probes or analytical tools designed to identify the gene of interest or the protein encoded by it. For cDNA expression **libraries**, suitable probes include monoclonal or polyclonal antibodies that recognize and specifically bind to HRG; oligonucleotides of about 20-80 bases in length that encode known or suspected portions of HRG cDNA from the **same** or **different species**; and/or complementary or homologous cDNAs or fragments thereof that encode the **same** or a hydridizing gene. Appropriate probes for screening genomic DNA **libraries** include, but are not

.mited to, oligonucle[redacted]ides; cDNAs or fragments thereof that encode the **ame** or hybridizing DN[redacted]and/or homologous genomic DNAs[redacted] fragments .hereof. Screening the cDNA or genomic **library** with the selected probe may be conducted using standard procedures as described in chapters 10-12 of Sambrook et al., supra.

US PAT NO: 5,304,640 :IMAGE AVAILABLE: L2: 26 of 36

DETDESC:

DETD(61)

Libraries are screened with probes designed to identify the gene of interest or the protein encoded by it. For cDNA expression **libraries**, suitable probes usually include mono- and polyclonal antibodies that recognize and specifically bind to the desired protein; oligonucleotides of about 20-80 bases in length that encode known or suspected portions of the selectin ligand cDNA from the **same** or **different species**; and/or complementary or homologous cDNAs or their fragments that encode the **same** or similar gene.

US PAT NO: 5,286,654 :IMAGE AVAILABLE: L2: 27 of 36

DETDESC:

DETD(40)

Libraries are screened with probes designed to identify the gene of interest or the protein encoded by it. For cDNA expression **libraries**, suitable probes include monoclonal or polyclonal antibodies that recognize and specifically bind to the TSF receptor; oligonucleotides of about 20-80 bases in length that encode known or suspected portions of the TSF receptor cDNA from the **same** or **different species**; and/or complementary or homologous cDNAs or fragments thereof that encode the **same** or a similar gene. Appropriate probes for screening genomic DNA **libraries** include, but are not limited to, oligonucleotides, cDNAs, or fragments thereof that encode the **same** or a similar gene, and/or homologous genomic DNAs or fragments thereof. Screening the cDNA or genomic **library** with the selected probe may be conducted using standard procedures as described in chapters 10-12 of Sambrook et al., supra.

US PAT NO: 5,279,960 :IMAGE AVAILABLE: L2: 28 of 36

DETDESC:

DETD(252)

To identify clones encoding coccidial antigens, cDNA **library** VII was screened with a mixture of monoclonal antibodies. Several phage plaques giving a positive reaction with the **pooled** MCAs were identified. Subsequent screenings of these positive plaques with individual MCAs resulted in the identification of plaques that react. . . . The monoclonal antibody was prepared against Eimeria acervulina and reacts with the refractile body in sporozoites of at least nine **different** Eimeria **species**. The monoclonal antibody inhibits the development of Eimeria in vitro. (Danforth, N.D., "Use of hybridoma antibodies combined with genetic engineering. . .

DETDESC:

DETD(253)

The genomic DNA **library** prepared in Example XII was also screened with the **pooled** monoclonal antibodies. This **library** was prepared

with mung bean nuclease treated Eimeria tenella DNA, and is cloned in .lambda.gtll. A clone which was initially identified with the **pooled** monoclonal antibodies was subsequently shown to produce an antigen which reacts specifically with monoclonal antibody 12-07. This monoclonal antibody was prepared against Eimeria acervulina and reacts with the sporozoite surface of at least nine **different** Eimeria **species**. The new antigen was designated GX3276. For DNA sequence analysis the cloned Eimeria DNA was transferred to M13 and the. . .

US PAT NO: 5,223,408 :IMAGE AVAILABLE: L2: 29 of 36

DETDESC:

DETD(77)

Libraries are screened with probes designed to identify either DNA encoding or the desired protein, or the desired protein itself. For cDNA expression **libraries**, suitable probes include monoclonal or polyclonal antibodies that recognize and specifically bind to the desired protein; oligonucleotides of about 20-80 bases in length that encode known or suspected portions of the desired protein cDNA from the **same** or **different species**; and/or complementary or homologous cDNAs or fragments thereof that encode the **same** or a similar gene. Appropriate probes for screening genomic DNA **libraries** include, but are not limited to, oligonucleotides; cDNAs or fragments thereof that encode the **same** or a similar gene; and/or homologous genomic DNAs or fragments thereof. Screening the cDNA or genomic **library** with the selected probe may be conducted using standard procedures as described in chapters 10-12 of Sambrook et al., supra.

US PAT NO: 5,216,126 :IMAGE AVAILABLE: L2: 30 of 36

DETDESC:

DETD(40)

Libraries are screened with probes designed to identify the gene of interest or the protein encoded by it. For cDNA expression **libraries**, suitable probes include monoclonal or polyclonal antibodies that recognize and specifically bind to the TSF receptor; oligonucleotides of about 20-80 bases in length that encode known or suspected portions of the TSF receptor cDNA from the **same** or **different species**; and/or complementary or homologous cDNAs or fragments thereof that encode the **same** or a similar gene. Appropriate probes for screening genomic DNA **libraries** include, but are not limited to, oligonucleotides, cDNAs, or fragments thereof that encode the **same** or a similar gene, and/or homologous genomic DNAs or fragments thereof. Screening the cDNA or genomic **library** with the selected probe may be conducted using standard procedures as described in chapters 10-12 of Sambrook et al., supra.

US PAT NO: 5,202,428 :IMAGE AVAILABLE: L2: 31 of 36

DETDESC:

DETD(23)

Because mitogenic proteins from **different** mammalian **species** usually show high homologies, i.e., porcine, human, bovine, ovine and rat, it appears certain that such homologous mitogens from other species can be deduced using the **same** probes as were employed in searching the rat cDNA **libraries**. Alternatively, cDNA fragments of the gene sequence coding for the rat mitogen (or the entire sequence) can be used to probe the cDNA **library** of another species, e.g., human. Thus, the knowledge of the sequence of the rat mitogen allows the present-day

molecular biologist. . . .

US PAT NO: 5,182,375 :IMAGE AVAILABLE: L2: 32 of 36

DETDESC:

DETD(22)

Because the inhibins from **different species** show great homologies, i.e., porcine, human, bovine, ovine and rat, it appeared certain that such homologous follistatins from other species could be deduced using the **same** probes as were employed in searching the porcine cDNA **libraries**. Alternatively, probes can be prepared using cDNA fragments of the gene sequence coding for porcine follistatin. Thus, the knowledge of. . .

US PAT NO: 5,182,205 :IMAGE AVAILABLE: L2: 33 of 36

DETDESC:

DETD(3)

Alternatively a nucleotide sequence which is selectively expressed in pre-B cells may be identified by screening a cDNA **library** with a homologous nucleotide sequence from another species, which nucleotide sequence has been identified by subtraction hybridization as described above. Suitable cDNA **libraries** are described in the Example. Homologous nucleotide sequences are nucleotide sequences with the **same** function but originating from **different species** and with practically a identical nucleotide sequence.

US PAT NO: 5,154,921 :IMAGE AVAILABLE: L2: 34 of 36

SUMMARY:

BSUM(10)

By . . . et al. (1987, 1988), but also any comparably active GRO endogenous to any animal species (particularly mammals or other vertebrate **species**). Three **different** human gro cDNAs have been cloned. Anisowicz et al. (1987) identified the first (now termed gro .alpha.) from a human bladder carcinoma cell line (T24) cDNA **library**. An adherent monocyte cDNA **library** probed with gro .alpha. cDNA yielded an 880 bp partial cDNA clone, the sequence of which differed somewhat from that of gro .alpha. cDNA; this partial cDNA was used to probe a second cDNA **library**, producing positively-hydridizing clones representing gro .alpha. cDNA and two variants termed gro .beta. and gro .gamma.. Partial sequence analysis of genomic clones obtained by probing a human genomic DNA **library** with gro .alpha. cDNA confirmed that the three forms are derived from related but different genes, all three of which appear to map to the **same** region of chromosome 4q. The nucleotide sequences and predicted translation sequences of the three cDNAs are compared in FIG. 2.

US PAT NO: 5,057,417 :IMAGE AVAILABLE: L2: 35 of 36

DETDESC:

DETD(160)

DNA . . . due to multiple differentially spliced RNA's at the 5' end of both these genes. The observation that clones from two **different species** isolated from a number of different cDNA **libraries** diverge at the **same** point suggests that this is not some unusual cloning artifact. Whether these differentially spliced clones are

›iologically significant will await. . .

US PAT NO: 5,041,538 :IMAGE AVAILABLE: L2: 36 of 36

DETDESC:

DETD(23)

Because the inhibins from **different species** show great homologies, i.e., porcine, human, bovine, ovine and rat, it appeared certain that such homologous follistatins from other species could be deduced using the **same** probes as were employed in searching the porcine cDNA **libraries**. Alternatively, probes can be prepared using cDNA fragments of the gene sequence coding for porcine follistatin. Thus, the knowledge of. . .

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E12         13      FOSTER L J/AU

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E22          5      FOSTER L W/AU
E23        145      FOSTER M/AU
E24        186      FOSTER M A/AU

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L5          26 FILE BIOSIS

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L5           26 FILE BIOSIS
     TOTAL FOR ALL FILES
L6           47 S E16
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E2            2      PETERSON SWEENEY K L/AU
E3          153 --> PETERSON T/AU
E4           67      PETERSON T A/AU
E5            1      PETERSON T B/AU
E6           81      PETERSON T C/AU
E7           10      PETERSON T D/AU
E8           37      PETERSON T E/AU
E9            3      PETERSON T F/AU
E10          15      PETERSON T G/AU
E11           3      PETERSON T H/AU
E12          10      PETERSON T J/AU

=> s e6

L1           24 FILE MEDLINE
L2           57 FILE BIOSIS

TOTAL FOR ALL FILES
L3           81 "PETERSON T C"/AU

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E6           42      FOSTER L B/AU
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=> d 1-13 bib ab

L13 ANSWER 1 OF 13 BIOSIS COPYRIGHT 1997 BIOSIS
AN 96:302090 BIOSIS
DN 99024446
TI Pentoxifylline, but not UDCA or TUDCA inhibits fibroproliferative activity of PBC patient sera samples.
AU ***Peterson T C*** ; Huet P M
CS Dep. Med., Dalhousie Univ., Halifax, NS, Canada
SO 96th Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week, San Francisco, California, USA, May 19-22, 1996. Gastroenterology 110 (4 SUPPL.). 1996. A1294. ISSN: 0016-5085
DT Conference
LA English

L13 ANSWER 2 OF 13 BIOSIS COPYRIGHT 1997 BIOSIS
AN 96:300878 BIOSIS
DN 99023234
TI Effect of pentoxifylline in collagenous colitis: A new therapy?.
AU ***Peterson T C*** ; Tanton R T
CS G.I. Div., Dep. Med., Dalhousie Univ., Halifax, NS, Canada
SO 96th Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week, San Francisco, California, USA, May 19-22, 1996. Gastroenterology 110 (4 SUPPL.). 1996. A990. ISSN: 0016-5085
DT Conference
LA English

L13 ANSWER 3 OF 13 MEDLINE DUPLICATE 1
AN 96186638 MEDLINE
TI Drug treatment of functional dyspepsia: a systematic analysis of trial methodology with recommendations for design of future trials [see comments].
CM Comment in: Am J Gastroenterol 1996 Apr;91(4):628-9
AU Veldhuyzen van Zanten S J; Cleary C; Talley N J; ***Peterson T C*** ; Nyren O; Bradley L A; Verlinden M; Tytgat G N
CS Division of Gastroenterology, Department of Medicine, Dalhousie University, Halifax, Canada.
SO AMERICAN JOURNAL OF GASTROENTEROLOGY, ***(1996 Apr)*** 91 (4) 660-73.
Journal code: 3HE. ISSN: 0002-9270.
CY United States
DT Journal; Article; (JOURNAL ARTICLE) (META-ANALYSIS)
LA English

=> s l3 and l6

L7 [redacted] 0 FILE MEDLINE
L8 0 FILE BIOSIS

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nested terms that are not separated by a logical operator.

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FS Priority Journals; Cancer Journals
EM 9610
AB OBJECTIVES: To evaluate drug treatment of functional dyspepsia (including Helicobacter pylori) and provide guidelines for future trials based on a critical systematic overview of published studies. METHODS: Data sources were a Medline search for articles published in English going back to 1966 and a manual search of four GI journals going back to 1980. Original randomized, double-blind, placebo-controlled trials were selected that enrolled at least 20 patients. Using a standardized, pretested data extraction form, studies were evaluated independently by two observers for study design, outcome measures, and results. RESULTS: Fifty two eligible studies were evaluated. Many studies suffered from important weaknesses in study design and execution. Only five studies used previously validated outcome measures. CONCLUSIONS: Because of suboptimal design and/or unclear presentation of the data, none of the trials provided unequivocal evidence that there is efficacious therapy for the treatment of functional dyspepsia.

L13 ANSWER 4 OF 13 MEDLINE DUPLICATE 2
AN 96319667 MEDLINE
TI Inhibition of fibroproliferation by pentoxifylline. Activity of metabolite-1 and lack of role of adenosine receptors.
AU ***Peterson T C***
CS Department of Medicine, Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada.
SO BIOCHEMICAL PHARMACOLOGY, ***(1996 Aug 23)*** 52 (4) 597-602. Journal code: 9Z4. ISSN: 0006-2952.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9611
AB We have reported previously that pentoxifylline and adenosine decrease platelet-derived growth factor- (PDGF) stimulated fibroproliferation. To determine the role of adenosine receptors in the inhibition of fibroproliferation observed with pentoxifylline, we used a non-selective adenosine receptor antagonist, 8-phenyltheophylline, and specific A1 and A2 adenosine receptor antagonists. If the A2 receptor, which is present on fibroblasts, mediates the inhibition of fibroproliferation which occurs with pentoxifylline, then pretreatment of fibroblasts with receptor antagonists prior to the addition of pentoxifylline should prevent the action of pentoxifylline. The results indicated that pretreatment of fibroblasts with 8-phenyltheophylline (100 microM) did not alter the inhibitory effect of pentoxifylline on PDGF-stimulated fibroproliferation. These results argue against a

mechanism involving inhibition of adenosine reuptake as the mechanism for pentoxifylline's effect in this system. 8-Phenyltheophylline also did not alter the effect of pentoxifylline on baseline proliferation, suggesting that these effects of pentoxifylline are not mediated by adenosine receptors. Pentoxifylline is metabolized to several metabolites including 1-(5-hydroxyhexyl)-3,7-dimethylxanthine (metabolite-1). Metabolite-1 significantly reduced PDGF-stimulated fibroproliferation and was as effective as pentoxifylline. The combination of pentoxifylline and metabolite-1 had an additive effect. Metabolite-1 and pentoxifylline also reduced baseline proliferation. Preincubation of fibroblasts with 8-phenyltheophylline did not prevent the inhibitory action of metabolite-1 on PDGF-stimulated proliferation or on basal proliferation of fibroblasts, suggesting that the action of metabolite-1 on fibroproliferation was not mediated by adenosine receptors. Results using A1 and A2 adenosine receptor antagonists further suggest that the effect of pentoxifylline was not mediated by adenosine receptors.

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AN 96:559231 BIOSIS
DN 99281587
TI Hepatic fibrosis as assessed by collagen deposition in AHR knockout mice compared to three animal models of fibrosis.
AU ***Peterson T C*** ; Fernandez-Salguero P; Gonzalez F J
CS Dep. Med. Pharmacol., Dalhousie Univ., Halifax, N.S., Canada
SO 47th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases, Chicago, Illinois, USA, November 8-12, 1996. Hepatology 24 (4 PART 2). 1996. 561A. ISSN: 0270-9139
DT Conference
LA English

L13 ANSWER 6 OF 13 BIOSIS COPYRIGHT 1997 BIOSIS
AN 96:273395 BIOSIS
DN 98829524
TI Effect of pentoxifylline in rat and swine models of hepatic fibrosis: Role of fibroproliferation in its mechanism.
AU ***Peterson T C*** ; Neumeister M
CS Sir Charles Tupper Med. Build., Rm 11-C1 Dalhousie Univ., Halifax, N.S. B3H 4H7, Canada
SO Immunopharmacology 31 (2-3). 1996. 183-193. ISSN: 0162-3109
LA English
AB Fibroproliferation was studied in two animal models of liver disease. Oral feeding of yellow phosphorus to pigs reproducibly results in fibrosis after 8 weeks of feeding, extensive fibrosis after 12 weeks and cirrhosis after 16 weeks of yellow phosphorus. Bile duct ligation

was used to induce cirrhosis in the rat. Fibroproliferation was assessed as uptake of tritiated thymidine into fibroblasts which had been incubated with monocyte-conditioned medium obtained from monocytes of pigs treated with yellow phosphorus or bile duct-ligated rats and compared to the corresponding controls. Fibrosis was assessed by collagen content of liver sections obtained from the two animal models. The collagen content was determined by quantitation of Sirius red/Fast green-stained liver sections. In both animal models collagen content was significantly elevated at the conclusion of the treatment. Collagen content of liver sections of yellow phosphorus-treated animals were elevated (40 +- 2.7, n = 15) compared to mineral oil-treated controls (23 +- 1.2, n = 12) and collagen levels in the bile duct-ligated rat model liver sections were elevated (31.2 +- 1.6, n = 6) compared to sham-operated controls (21.6 +- 0.7, n = 6). The results of the fibroproliferation assay indicate that monocytes obtained from pigs treated with yellow phosphorus produce fibroproliferative factors during the development of fibrosis. This is in contrast to the bile duct-ligated rat model where no differences were observed in the production of fibroproliferative factors in the bile duct-ligated rats compared to sham operated controls suggesting that this may not be a key event in this model of fibrosis. Pentoxifylline treatment of the yellow phosphorus induced swine model of hepatic fibrosis has been associated with a marked improvement in fibrosis. In this study treatment of fibrotic pigs with pentoxifylline was associated with an improvement in liver function tests, a reduction of collagen content of liver sections, and reduction in fibroproliferation in pigs receiving yellow phosphorus treatment. Fibroproliferative factors were produced during the development of fibrosis in the swine model of fibrosis and their effect was blocked by pentoxifylline administered in vivo. This is in contrast to the bile duct-ligated rat model where pentoxifylline treatment was not associated with improvement in liver function tests or reduction of collagen content of liver sections and did not alter the fibroproliferative activity of monocyte-conditioned media. Taken together these results suggest that fibroproliferation and increased synthesis of collagen are key events in the yellow phosphorus-induced pig model of hepatic fibrosis and that the action of pentoxifylline in this animal model is likely to be related to its effects on fibroproliferation with a subsequent effect on collagen production. This is in contrast to the bile duct-ligated rat model where the results from this study suggest that fibroproliferation per se does not appear to be a key event and where pentoxifylline treatment does not alter fibroproliferative activity nor after the course of fibrosis in this animal model.

L13 ANSWER 7 OF 13 BIOSIS COPYRIGHT 1997 BIOSIS
AN 95:282133 BIOSIS

DN 98296433
TI Combination of pentoxifylline and UDCA blocks proliferation of human fibroblasts.
AU ***Peterson T C*** ; White B
CS Dep. Med., Dalhousie Univ., Halifax, NS, Canada
SO 95th Annual Meeting of the American Gastroenterological Association and Digestive Disease Week, San Diego, California, USA, May 14-17, 1995. Gastroenterology 108 (4 SUPPL.). 1995. A1146. ISSN: 0016-5085
DT Conference
LA English

L13 ANSWER 8 OF 13 BIOSIS COPYRIGHT 1997 BIOSIS
AN 95:281125 BIOSIS
DN 98295425
TI Quantitation of collagen in colonic sections from control and TNBS treated rats.
AU ***Peterson T C*** ; Davidson G; White B
CS Dep. Med., Dalhousie Univ., Halifax, NS H3H BH7, Canada
SO 95th Annual Meeting of the American Gastroenterological Association and Digestive Disease Week, San Diego, California, USA, May 14-17, 1995. Gastroenterology 108 (4 SUPPL.). 1995. A893. ISSN: 0016-5085
DT Conference
LA English

L13 ANSWER 9 OF 13 BIOSIS COPYRIGHT 1997 BIOSIS
AN 95:523486 BIOSIS
DN 98537786
TI Role of adenosine receptors in the inhibition of fibroproliferation due to pentoxifylline and M-1 metabolite.
AU ***Peterson T C*** ; White B
CS Dep. Med., Dalhousie Univ., Halifax, N.S., Canada
SO 46th Annual Meeting and Postgraduate Course of the American Association for the Study of Liver Diseases, Chicago, Illinois, USA, November 3-7, 1995. Hepatology 22 (4 PART 2). 1995. 475A. ISSN: 0270-9139
DT Conference
LA English

L13 ANSWER 10 OF 13 BIOSIS COPYRIGHT 1997 BIOSIS
AN 95:523485 BIOSIS
DN 98537785
TI Fibroproliferation in swine and rat models: Effect of pentoxifylline.
AU ***Peterson T C*** ; Neumeister M
CS Dep. Med., Dalhousie Univ., Halifax, N.S., Canada
SO 46th Annual Meeting and Postgraduate Course of the American Association for the Study of Liver Diseases, Chicago, Illinois, USA, November 3-7, 1995. Hepatology 22 (4 PART 2). 1995. 474A. ISSN:

0270-9139
DT Conference
LA English

L13 ANSWER 11 OF 13 BIOSIS COPYRIGHT 1997 BIOSIS
AN 95:523484 BIOSIS
DN 98537784
TI Expression of CYP1A1 and CYP1A2 in the yellow phosphorus induced swine model of hepatic fibrosis and the bile duct ligated rat.
AU ***Peterson T C*** ; Chen D K; Cheung C H
CS Dep. Med., Dalhousie Univ., Halifax, N.S., Canada
SO 46th Annual Meeting and Postgraduate Course of the American Association for the Study of Liver Diseases, Chicago, Illinois, USA, November 3-7, 1995. Hepatology 22 (4 PART 2). 1995. 474A. ISSN: 0270-9139
DT Conference
LA English

L13 ANSWER 12 OF 13 BIOSIS COPYRIGHT 1997 BIOSIS
AN 95:523305 BIOSIS
DN 98537605
TI Effect of pentoxifylline in a heterologous serum model of fibrosis in the rat.
AU Hodgson P D; ***Peterson T C***
CS Dep. Pharmacol., Dalhousie Univ., Halifax, NS, Canada
SO 46th Annual Meeting and Postgraduate Course of the American Association for the Study of Liver Diseases, Chicago, Illinois, USA, November 3-7, 1995. Hepatology 22 (4 PART 2). 1995. 429A. ISSN: 0270-9139
DT Conference
LA English

L13 ANSWER 13 OF 13 BIOSIS COPYRIGHT 1997 BIOSIS
AN 95:522710 BIOSIS
DN 98537010
TI Effect of PDGF, pentoxifylline and metabolite-1 on collagen production in porcine hepatic stellate cells.
AU Isbrucker R A; ***Peterson T C***
CS Dalhousie Univ., Dep. Pharmacol., Halifax, NS, Canada
SO 46th Annual Meeting and Postgraduate Course of the American Association for the Study of Liver Diseases, Chicago, Illinois, USA, November 3-7, 1995. Hepatology 22 (4 PART 2). 1995. 280A. ISSN: 0270-9139
DT Conference
LA English

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(FILE 'HOME' ENTERED AT 15:52:23 ON 15 MAY 1997)

FILE 'MEDLINE, BIOSIS' ENTERED AT 15:52:33 ON 15 MAY 1997
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L1 24 FILE MEDLINE
L2 57 FILE BIOSIS
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L3 81 S E6
E FOSTER L/AU
L4 21 FILE MEDLINE
L5 26 FILE BIOSIS
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L6 47 S E16
L7 0 FILE MEDLINE
L8 0 FILE BIOSIS
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L9 0 S L3 AND L6
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L11 13 FILE BIOSIS
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L12 15 S L3 AND PY=>1995
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L14 6 FILE MEDLINE

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L17 12 DUPLICATE REMOVE L16 (5 DUPLICATES REMOVED)

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L17 ANSWER 1 OF 12 MEDLINE DUPLICATE 1

AN 96388220 MEDLINE
TI Bcl-2 expression in neural cells blocks activation of ICE/CED-3 family proteases during apoptosis.
AU Srinivasan A; ***Foster L M*** ; Testa M P; Ord T; Keane R W; Bredesen D E; Kayalar C
CS Program on Aging, Burnham Institute, La Jolla, California 92037, USA.
NC AG 12282 (NIA)
NS 25554 (NINDS)
SO JOURNAL OF NEUROSCIENCE, ***(1996 Sep 15)*** 16 (18) 5654-60.
Journal code: JDF. ISSN: 0270-6474.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9702
EW 19970204
AB The ICE/CED-3 family of proteases has been implicated in playing a fundamental role in programmed cell death. Bcl-2 protein represses a number of apoptotic death programs, but the biochemical mechanism of its action is not known. We investigated the activation of ICE/CED-3 proteases induced by three apoptotic stimuli (staurosporine, ceramide, and serum withdrawal) in the neuronal cell line GT1-7 and in cells overexpressing Bcl-2. Rapid activation of a 17 kDa subunit of an activated member of the ICE/CED-3 family is demonstrated by affinity-labeling GT1-7 extracts from apoptotic controls cells with a biotinylated ICE/CED-3 inhibitor. This activation corresponds to an increased ICE/CED-3-like protease activity in extracts measured by a fluorogenic substrate assay. In a cell-free system, these extracts induce apoptotic morphological changes in intact nuclei. All three activities are readily inhibited by treatment of control extracts with ICE/CED-3-like protease inhibitors. Overexpressed Bcl-2 inhibits the activation of the 17 kDa protein, the ICE/CED-3-like protease activity in the fluorogenic assay, and the induction of apoptotic morphological changes in HeLa nuclei in the cell-free system, similar to results obtained with ICE/CED-3 protease inhibitors. At the mRNA level, overexpression of Bcl-2 did not alter expression of five members of the ICE/CED-3 family: CPP32, ICE, Mch 2, Nedd 2, and TX. Overexpression of Bcl-2 prevented the apoptosis-induced processing of pro-Nedd 2 to the cleaved form. These data suggest that Bcl-2 participates upstream from the function of ICE/CED-3 proteases and may inhibit apoptosis by preventing the post-translational activation of ICE/CED-3 proteases.

L17 ANSWER 2 OF 12 BIOSIS COPYRIGHT 1997 BIOSIS
AN 96:505148 BIOSIS
DN 99227504

TI A nematode larval motility inhibition assay for screening plant extracts and natural products.

AU Lorimer S D; Perry N B; ***Foster L M*** ; Burges E J; Douch P G C; Hamilton M C; Donaghy M J; McGregor R A

CS Plant Extracts Res. Unit, New Zealand Inst. Corp Food Res. Ltd., Dep. Chem., Univ. Otago, PO Box 56, Dunedin, New Zealand

SO Journal of Agricultural and Food Chemistry 44 (9). 1996. 2842-2845. ISSN: 0021-8561

LA English

AB An in vitro nematode larval motility inhibition assay has been developed to screen plant extracts for anthelmintic activity against the sheep parasite Trichostrongylus colubriformis. The usefulness of this assay was verified by results for extracts of the liverwort Plagiochila stephensoniana and the shrub Pseudowintera colorata. The activity of these extracts was due to 4-hydroxy-3'-methoxybibenzyl (1) (IC-50 0.13 mg/mL) and polygodial (2) (IC-50 0.07 mg/mL), respectively. Synthetic analogues of 1 displayed enhanced antiparasitic activity. (Z)-4-Hydroxy-3'-methoxystilbene (3) had an IC-50 of 0.06 mg/mL. The activity of an extract of the tree Phyllocladus aspeniifolius var. alpinus was due to the presence of polyphenolics, since treatment of the extract with polyvinylpolypyrrolidone or polyamide removed the activity.

L17 ANSWER 3 OF 12 BIOSIS COPYRIGHT 1997 BIOSIS

AN 97:34194 BIOSIS

DN 99340597

TI Infraspecific variation of insecticidal sesquiterpene dialdehydes in Pseudowintera colorata.

AU Perry N B; ***Foster L M*** ; Lorimer S D

CS Plant Extracts Res. Unit, New Zealand Inst. Crop Food Res. Ltd., Dep. Chem., Univ. Otago, P.O. Box 56, Dunedin, New Zealand

SO Phytochemistry (Oxford) 43 (6). 1996. 1201-1203. ISSN: 0031-9422

LA English

AB HPLC and NMR methods are described for determining the levels of the sesquiterpene dialdehydes polygodial and 9-deoxymuzigadial in the foliage of Pseudowintera colorata. Analyses of 25 individual plants, from four populations on the South Island of New Zealand, showed two chemotypes: a mixed chemotype with similar levels of polygodial and 9-deoxymuzigadial, and a polygodial chemotype with very low levels of 9-deoxymuzigadial. Only the polygodial chemotype was found in northern and southwestern populations, both chemotypes were found in a central eastern population, and only the mixed chemotype was found in a southeastern population.

L17 ANSWER 4 OF 12 MEDLINE

AN 96384735 MEDLINE

TI Isoprenyl phenyl ethers from liverworts of the genus Trichocolea:

cytotoxic activity, structural corrections, and synthesis.
AU Perry N B; ***Foster L M*** ; Lorimer S D; May B C; Weavers R T
CS Plant Extracts Research Unit, New Zealand Institute for Crop & Food Research Limited, Dunedin, New Zealand.. perryn@alkali.otago.ac.nz
SO JOURNAL OF NATURAL PRODUCTS, ***(1996 Aug)*** 59 (8) 729-33. Journal code: JA4. ISSN: 0163-3864.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9703
EW 19970304
AB The main cytotoxic component in New Zealand collections of the liverwort Trichocolea mollissima was identified as methyl 4-[(5-oxogeranyl)oxy]-3-methoxybenzoate, a structure that has not been reported previously. Two double-bond isomers of this geranyl ether were present at lower levels. Reinvestigation of the benzoates from Japanese collections of Trichocolea tomentella led to the identification of four geranyl ethers (including two of the three compounds identified from T. mollissima), which had previously been assigned incorrect geranyl ester structures. One compound, previously reported as a 3,3-dimethylallyl ester, could not be reisolated from T. tomentella, but was found in a New Zealand collection of Trichocolea lanata. It was shown to be a 3,3-dimethylallyl ether by synthesis from methyl vanillate. Several of these compounds were active in cytotoxic and antifungal assays.

L17 ANSWER 5 OF 12 BIOSIS COPYRIGHT 1997 BIOSIS
AN 96:564916 BIOSIS
DN 99294272
TI Conditionally immortalized neural cell lines: Potential models for the study of neural cell function.
AU Bongarzone E R; ***Foster L M*** ; Byravan S; Verity A N; Landry C F; Schonmann V; Amur-Umarjee S; Campagnoni A T
CS Dev. Biol. Group, Mental Retardation Res. Cent., Neuropsychychiatric Hosp. Inst., Univ. Calif., Los Angeles Medical Sch., 760 Westwood Plaza, Los Angeles, CA 90095, USA
SO Methods (Orlando) 10 (3). 1996. 489-500. ISSN: 1046-2023
LA English
AB Studies on primary cell cultures have contributed significantly to our understanding of neural cell function. Nevertheless, for many studies the value of these primary cell cultures has been limited by the time the cultures survive in vitro, the quantity of cellular material available for analysis, and the need to prepare the cells on a regular basis from fresh tissue. Techniques for immortalizing cells have existed for some time, but the repertoire of immortalizing genes has grown significantly. This has expanded our ability to generate

useful cell lines of specific neural types that are better models of the in vivo phenotype than previously. The constitutive expression of oncogenes keeps cells in a proliferative state that could lead to the loss of differentiated gene expression and function. An appealing improvement of immortalization methodology is the use of temperature-sensitive oncogenes that generate cell lines that can proliferate at a permissive temperature and "differentiate" at a nonpermissive temperature. The proliferation of such conditionally immortalized cell lines can be suppressed simply by increasing the temperature. Cell lines maintained at the nonpermissive temperature can enter into a stage in which they express differentiated properties of the cell. The potential ability of conditionally immortalized neural cell lines to accurately reflect their in vivo function has now been demonstrated on several occasions through transplantation experiments. In this report, the generation of these cell lines is described along with a discussion of their potential applications in neurobiology.

L17 ANSWER 6 OF 12 MEDLINE DUPLICATE 2
AN 96333157 MEDLINE
TI The glycosidic precursor of (Z)-5-ethylidene-2(5H)-furanone in Halocarpus biformis juvenile foliage.
AU Perry N B; Benn M H; ***Foster L M*** ; Routledge A; Weavers R T
CS Department of Chemistry, University of Otago, New Zealand.
SO PHYTOCHEMISTRY, ***(1996 May)*** 42 (2) 453-9.
Journal code: ALB. ISSN: 0031-9422.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; B
EM 9610
AB A new glycosidic lactone, (5R,6R)-5-(1-hydroxyethyl)-2(5H)-furanone beta-D-glucopyranoside, has been identified as the principal precursor of (Z)-5-ethylidene-2(5H)-furanone in juvenile foliage of the New Zealand tree Halocarpus biformis. Three related lactone glycosides were isolated in smaller amounts, together with the known phenolic glycosides pyroside, arbutin and picein. The principal lactone glycoside underwent facile elimination of glucose, in neutral or basic conditions, to yield (Z)-5-ethylidene-2(5H)-furanone and its E-isomer. This lactone glycoside was also detected in foliage of H. bidwillii and H. kirkii.

L17 ANSWER 7 OF 12 MEDLINE DUPLICATE 3
AN 96054084 MEDLINE
TI Sesquiterpene/quinol from a New Zealand liverwort, Riccardia crassa.
AU Perry N B; ***Foster L M***
CS New Zealand Institute for Crop & Food Research Limited, Department

of Chemistry, University of Otago, Dunedin, New Zealand.
SO JOURNAL OF NATURAL PRODUCTS, ***(1995 Jul)*** 58 (7) 1131-5.
Journal code: JA4. ISSN: 0163-3864.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9601
AB A new sesquiterpene/quinol, with mild cytotoxic and antibacterial activity, has been isolated from a New Zealand collection of the liverwort Riccardia crassa. The structure of this compound, riccardiphenol C [3], was established by nmr spectroscopy. Closely related compounds previously isolated from a Japanese collection of R. crassa were not detected in this collection.

L17 ANSWER 8 OF 12 BIOSIS COPYRIGHT 1997 BIOSIS
AN 96:114069 BIOSIS
DN 98686204
TI Effects of podocarp extracts on lettuce seed germination and seedling growth.
AU Perry N B; ***Foster L M*** ; Jameson P E
CS Plant Extract Res. Unit, New Zealand Inst. Crop Food Res. Limited, Dep. Chem., Univ. Otago, P.O. Box 56, Dunedin, New Zealand
SO New Zealand Journal of Botany 33 (4). 1995. 565-568. ISSN: 0028-825X
LA English
AB The effects of ethanol extracts from 16 of the 17 New Zealand species in the family Podocarpaceae on the germination of lettuce seeds and hypocotyl elongation are reported. Extracts of both juvenile and adult forms of Halocarpus kirkii and Halocarpus bidwillii were tested. Each extract was tested at three different levels: undiluted, and diluted times 10-3 and times 10-6. The effects on germination and hypocotyl elongation were compared with solvent controls. None of the extracts showed promotion of hypocotyl elongation, so no gibberellin-like activity was detected. The majority of the undiluted podocarp extracts inhibited both germination and hypocotyl elongation.

L17 ANSWER 9 OF 12 MEDLINE DUPLICATE 4
AN 96119884 MEDLINE
TI Conditionally immortalized oligodendrocyte cell lines migrate to different brain regions and elaborate 'myelin-like' membranes after transplantation into neonatal shiverer mouse brains.
AU ***Foster L M*** ; Landry C; Phan T; Campagnoni A T
CS Mental Retardation Research Center, UCLA School of Medicine 90024, USA.
NC NS23322 (NINDS)
NS23022 (NINDS)

NS09192 (NINDS)
SO DEVELOPMENTAL NEUROSCIENCE, ***(1995)*** 17 (3) 160-70.
Journal code: EC5. ISSN: 0378-5866.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9604
AB Five immortalized oligodendrocyte cell lines, representing a spectrum of different stages of oligodendrocyte maturation, were transplanted into neonatal shiverer mouse brains and examined for their ability to survive, multiply, and migrate in vivo. Each of the cell lines migrated to different regions of the brain with remarkable consistency when injected into the mouse forebrain, suggesting that the cells might be responding to different environmental cues present in the neonatal mouse brain. These results are consistent with the fact that cells at different stages in the oligodendrocyte lineage probably possess different sets of surface molecules and receptors. Significant differences were also observed in the survival and proliferation of the lines examined, even when the lines tested had quite similar in vitro phenotypes. Interestingly, the cell line with the most mature in vitro phenotype, N20.1, appeared to elaborate membranous processes when transplanted into the brain, reminiscent of oligodendrocytes ensheathing axonal segments. The experiments suggest that these immortalized cells could be useful models to study the cellular and molecular mechanisms involved in the development, maturation and possibly formation of myelin by oligodendrocytes in the mammalian brain.

L17 ANSWER 10 OF 12 MEDLINE DUPLICATE 5
AN 96001257 MEDLINE
TI Cloning and characterization of a G protein alpha-subunit-encoding gene from the basidiomycete, Coprinus congregatus.
AU Kozak K R; ***Foster L M*** ; Ross I K
CS Department of Biological Sciences, University of California, Santa Barbara 93106, USA.
SO GENE, ***(1995 Sep 22)*** 163 (1) 133-7.
Journal code: FOP. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X68031
EM 9601
AB Complementary DNA (cDNA) clones encoding two G protein alpha-subunit proteins (CGP alpha 1 and CGP alpha 2) were isolated from a Coprinus

[redacted]ngregatus (Cc) hyphal tip cell (HTC) library using PCR-generated [redacted]tinylated G protein probes. Sequence analysis of the Cc cgp alpha [redacted]ene indicates that the gene contains an open reading frame (ORF) [redacted]at translates into a putative 353-amino-acid (aa) product. The predicted CGP alpha 1 protein exhibits similarity to all known G protein alpha-subunits (it has all of the consensus regions for a GTP-binding protein), especially the mammalian retinal G protein, transducin. The CGP alpha 1 aa sequence is 50% identical overall to the transducin subfamily, cgp alpha 1 shares the same aa size grouping as transducin alpha-subunits and, unlike many other G proteins, both CGP alpha 1 and transducin seem to possess a cholera toxin (CTX)- and pertussis toxin (PTX)-sensitive site. Preliminary reverse transcription PCR (RT-PCR) analysis of cgp alpha 1 and cgp alpha 2 mRNA expression revealed that, unlike cgp alpha 2 which seems to be constitutively expressed, cgp alpha 1 is expressed only in HTC that are competent in responding to light. Thus, the cgp alpha 1 product, CGP alpha 1, is a likely candidate for regulating the blue light-induced signal transduction photomorphogenesis system found in Cc.

L17 ANSWER 11 OF 12 BIOSIS COPYRIGHT 1997 BIOSIS
AN 95:147645 BIOSIS
DN 98161945
TI Immortalization of glial cell lines from normal and jimpy mice.
AU Byravan S; ***Foster L M*** ; Amur-Umarjee S; Campagnoni A T
CS UCLA Sch. Med., 760 Westwood Plaza, Los Angeles, CA 90024, USA
SO Twenty-sixth Meeting of the American Society for Neurochemistry, Santa Monica, California, USA, March 5-9, 1995. Journal of Neurochemistry 64 (SUPPL. 1). 1995. S99. ISSN: 0022-3042
DT Conference
LA English

L17 ANSWER 12 OF 12 BIOSIS COPYRIGHT 1997 BIOSIS
AN 95:425946 BIOSIS
DN 98440246
TI Conditionally immortalized JIMPY oligodendrocytes exhibit temperature sensitive regulation of the expression of the PLP gene.
AU Bongarzone E R; Byravan S; ***Foster L M*** ; Kashima T; Campagnoni A T
CS UCLA Mental Retardation Research Center, Neuropsychiatric Inst., 760 Westwood Plaza, Los Angeles, CA 90024, USA
SO 25th Annual Meeting of the Society for Neuroscience, San Diego, California, USA, November 11-16, 1995. Society for Neuroscience Abstracts 21 (1-3). 1995. 41. ISSN: 0190-5295
DT Conference
LA English

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E5     USPAT                1     KHOSLA, CHAITAN/IN
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E7     USPAT                8     KHOSLA, MAHESH CHANDRA/IN
E8     USPAT                1     KHOSLA, MUKUL/IN
E9     USPAT                1     KHOSLA, PANKAJ/IN
E10    USPAT                3     KHOSLA, RAJINDER P/IN
E11    USPAT                1     KHOSRAVI, CHRISTOPHER H/IN
E12    USPAT                1     KHOSRAVI, FAHRAD/IN
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             1 "KHOSLA, CHAITAN"/IN
             1 "KHOSLA, CHAITAN S"/IN
L1           2 ("KHOSLA, CHAITAN"/IN OR  "KHOSLA, CHAITAN S"/IN)
=> d 1-2 bib ab


US PAT NO:      5,521,077 [IMAGE AVAILABLE]          L1: 1 of 2
DATE ISSUED:    May 28, 1996
TITLE:          Method of generating multiple protein variants and
                  populations of protein variants prepared thereby
INVENTOR:       **Chaitan Khosla**, Stanford, CA
                Robert Caren, Stanford, CA
ASSIGNEE:       The Leland Stanford Junior University, Palo Alto, CA (U.S.
                  corp.)
APPL-NO:        08/234,023
DATE FILED:     Apr. 28, 1994
ART-UNIT:       184
PRIM-EXMR:      James Martinell
LEGAL-REP:      Reed & Robins

US PAT NO:      5,521,077 [IMAGE AVAILABLE]          L1: 1 of 2

ABSTRACT:
A method based on generalized recombination is provided for generating
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multiple protein variants. The method involves introducing into host cells at least two pools of mutant encoding nucleotide sequences, recipient and donor, transducing the donor pool into the recipient cells and subsequently screening and selecting the recombinants thereby produced for expressed proteins exhibiting desired characteristics. A population of such protein variants is also provided.

L1: 2 of 2

US PAT NO: 5,049,493 [IMAGE AVAILABLE]
DATE ISSUED: Sep. 17, 1991
TITLE: Enhancement of cell growth by expression of a cloned hemoglobin gene
INVENTOR: **Chaitan S. Khosla**, Pasadena, CA
James E. Bailey, Pasadena, CA
ASSIGNEE: California Institute of Technology, Pasadena, CA (U.S. corp.)
APPL-NO: 07/342,451
DATE FILED: Jan. 24, 1989
ART-UNIT: 185
PRIM-EXMR: Richard A. Schwartz
ASST-EXMR: Mary E. Mosher
LEGAL-REP: Carolyn J. Adler, David W. Collins, Reginald J. Suyat

L1: 2 of 2

US PAT NO: 5,049,493 [IMAGE AVAILABLE]

ABSTRACT:

The invention relates to nucleotide sequences, including a substantially purified gene which codes for an oxygen-binding protein, and a gene promoter/regulator which is useful in subjecting the translation/transcription of DNA sequences to selective regulation by external control, and plasmid vectors containing those nucleotide sequences, which are valuable bioprocessing catalysts for enhancing the growth characteristics of cells, and increasing production of various proteins and metabolites of those cells. Methods for the use of these nucleotide sequences and related plasmids for a range of applications including oxygen supply to cells, growth enhancement, expression of various gene products, enhancement of oxygen-requiring processes, binding and separation of oxygen from liquids and gases, and a range of oxidative reactions are also disclosed.

=> s combinatorial (p) (gene or library)
2812 COMBINATORIAL
7 COMBINATORIALS
2812 COMBINATORIAL
(COMBINATORIAL OR COMBINATORIALS)
12526 GENE
8934 GENES

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      13684 GENE
                (GENE OR GENES)
      12103 LIBRARY
       4256 LIBRARIES
      13368 LIBRARY
                (LIBRARY OR LIBRARIES)
L2      174 COMBINATORIAL (P) (GENE OR LIBRARY)
=> s l2 (p) species
      93255 SPECIES
L3       11 L2 (P) SPECIES
=> d 1-11 kwic
```

US PAT NO: 5,608,046 [IMAGE AVAILABLE] L3: 1 of 11

SUMMARY:

BSUM(6)

Naturally occurring or synthetic oligonucleotides, together with hybrid **species** having both synthetic and natural components, can collectively be referenced as "oligomeric compounds." Because of their properties, these oligomeric compounds. . . in cloning, blotting procedures, and in applications such as fluorescence in situ hybridization (FISH). Also, since local triplex formation inhibits **gene** transcription, such oligomeric compounds can be used to inhibit **gene** transcription. Labeled oligomers can also be used to directly map DNA molecules, such as by tagging an oligomer with a. . . fluorescent label and effecting hybridization to complementary sequences in duplex DNA. Oligomers can also be used as identification tags in **combinatorial** chemical **libraries** as is disclosed in patent publication WO 94/08051 and Ohlmeyer et al., Proc. Natl. Acad. Sci. USA, 1993, 90, 10922-10926.

SUMMARY:

BSUM(80)

In . . . acid binding properties of the compounds of the invention can be used to form duplex structures with an unknown oligomer **species** for identification of that **species** by gel analysis including slab and capillary gel electrophoresis. In still further embodiments of the inventions, the compounds of the invention can be used as tags in identification of other compounds in **combinatorial** **libraries**.

US PAT NO: 5,605,616 [IMAGE AVAILABLE] L3: 2 of 11

DETDESC:

DETD(80)

Combinatorial **libraries** can be screened to determine whether any members of the **library** have a desired activity, and, if so, to identify the active **species**. Methods of screening **combinatorial** **libraries** have been described (see, e.g., Gordon et al., J Med Chem., op. cit.). Soluble compound **libraries** can be screened by affinity chromatography with an appropriate receptor to isolate ligands for the receptor, followed by identification of. . .

US PAT NO: 5,587,471 [IMAGE AVAILABLE] L3: 3 of 11

SUMMARY:

BSUM(5)

As compared to amino acids, nucleotide monomers and chemical **species** related thereto represent a very different class of chemicals having very different properties. These difference are of such extent so as to require very dissimilar chemistries to prepare polymeric **species** from the monomers. Additionally they present other problems and differences such as purification that must be overcome in the preparation of random **libraries**. Until now, little work has been done to optimize the preparation and use of nucleotide based **combinatorial** **libraries**. Huse, et al., PCT/US91/05939 filed Aug. 20, 1991, teach a method of synthesizing oligonucleotides having random tuplets (i.e. doublets, triplets,. . .

US PAT NO: 5,585,087 [IMAGE AVAILABLE] L3: 4 of 11

DETDESC:

DETD(20)

In . . . to promote the highest homology possible. Such a population of variants can include, for example, homologs from one or more **species**, as well as various isoforms from one **species**. For instance, the family of bone morphogenic proteins (BMPs), as well as other members of the Transforming Growth Factor-.beta. (TGF.beta.s), can be used to generate a **combinatorial** **library**. To analyze the sequences of a population of related proteins, the amino acid sequences (or nucleotide sequences) of interest can. . . be real or artificial. Analysis of the alignment of the proteins can give rise to the generation of a degenerate **library** of polypeptides comprising potential sequences based on conserved and nonconserved residues in each position

of the aligned sequences. A **combinatorial** **library** can then be produced by way of a degenerate **library** of **genes** encoding a **library** of polypeptides which each include at least a portion of potential protein sequences. For instance, a mixture of synthetic oligonucleotides can be enzymatically ligated into **gene** sequences such that the degenerate set of potential sequences are expressible as individual polypeptides.

US PAT NO: 5,574,017 [IMAGE AVAILABLE] L3: 5 of 11

DETDESC:

DETD(61)

Moreover, the compounds of the present invention, particularly **libraries** of variants having various representative classes of substituents, can be generated using **combinatorial** chemistry (see, for example, PCT WO 94/08051) and rapidly screened in high throughput assays in order to identify potential lead compounds for inhibiting the growth of a particular bacterial **species**. For instance, simple turbidimetric assays (e.g. measuring the A.sub.600 of a culture) can be used to assess the effects of. . .

US PAT NO: 5,573,905 [IMAGE AVAILABLE] L3: 6 of 11

DETDESC:

DETD(3)

An encoded **combinatorial** chemical **library** is a composition comprising a plurality of **species** of bifunctional molecules that each define a different chemical structure and that each contain a unique identifier oligonucleotide whose nucleotide. . .

US PAT NO: 5,539,083 [IMAGE AVAILABLE] L3: 7 of 11

DETDESC:

DETD(3)

Peptide . . . in binding affinity makes these peptide nucleic acid oligomers especially useful as molecular probes and diagnostic agents for nucleic acid **species**. Despite these known uses of peptide nucleic acids, it is not known to prepare peptide nucleic acid **libraries** or to use peptide nucleic acid monomers or sub-monomer in **combinatorial** techniques.

US PAT NO: 5,523,389 [IMAGE AVAILABLE] L3: 8 of 11

DETDESC:

DETD(52)

Although . . . Biomol. Str. Dyn. 9, 1131-1153; and Wang, Y. & Patel, D. J. (1992) Biochemistry 31, 8112-8119. The oligonucleotides in the **combinatorial** **library** pools that show antiviral activity (Table 1) and oligonucleotide ISIS 5320 form multimeric complexes as shown by size exclusion chromatography (FIG. 1). The retention time of the complex was that expected for a tetrameric **species** based on plots of retention time vs. log molecular weight of phosphorothioate oligonucleotide standards (data not shown). The circular dichroism. . . oligonucleotides of dissimilar size, but each containing four or five guanosines in a row, are incubated together, five distinct aggregate **species** are formed on a non-denaturing gel Sen, D. & Gilbert, W. (1990) Nature 344, 410-414 and Kim, J., Cheong, C.. . . oligonucleotide containing 4 guanosines near the 3' end (.sup.5' T.sub.13 G.sub.4 T.sub.4.sup.3' ; SEQ ID NO: 4), the five aggregate **species** expected for a parallel-stranded tetramer were observed on a non-denaturing gel (FIG. 2). Example 7

US PAT NO: 5,506,337 [IMAGE AVAILABLE] L3: 9 of 11

SUMMARY:

BSUM(35)

Since the chance of finding useful ligands increases with the size of the **combinatorial** **library**, it is desirable to generate **libraries** composed of large numbers of different-sequence oligomers. In the case of oligonucleotides, for example, a **library** having 4-base variability at 8 oligomer residue positions will contain as many as 4.sup.8 (65,536) different sequences. In the case of a polypeptides, a **library** having 20-amino acid variability at six residue positions will contain as many as 20.sup.6 (64,000,000) different **species**.

DETDESC:

DETD(81)

The **combinatorial** **libraries** described above are used to select one or more oligomer **species** in the **library** that demonstrate a specific interaction with a selected receptor. The receptor is any biological receptor of interest, that is, one. . .

US PAT NO: 5,498,531 [IMAGE AVAILABLE] L3: 10 of 11

DETDESC:

DETD(63)

Addition . . . be manipulated such that a variegated population of exons is heterologous with respect to intron binding sequences (e.g. one particular **species** of exon has a different IBS relative to other exons in the population). Thus, sequential addition of intronic RNA having discrete EBS sequences can reduce the construction of a **gene** to non-random or only semi-random assembly of the exons by sequentially activating only particular **combinatorial** units in the mixture. Another advantage derives from being able to store exons as part of a **library** without self-splicing occurring at any significant rate during storage. Until the exons are activated for trans-splicing by addition of the. . .

US PAT NO: 5,258,289 [IMAGE AVAILABLE] L3: 11 of 11

DETDESC:

DETD(12)

The general approach to construction of the **combinatorial** **libraries** is described in Example 1 and the required vectors are diagramed in FIG. 4. In brief, coding sequences for immunoglobulin. . . Suitable sources for the mRNA include B lymphocytes or plasma cells from any of a variety of tissues from any **species**: for example, mouse spleen cells or human peripheral blood lymphocytes. The choice of immunoglobin light chains of course depends on the **species** chosen as the mRNA source: for example for human, mouse, and rabbit mRNA sources, light chains are chosen from the. . .
=> d 10 bib ab

US PAT NO: 5,498,531 [IMAGE AVAILABLE] L3: 10 of 11
DATE ISSUED: Mar. 12, 1996
TITLE: Intron-mediated recombinant techniques and reagents
INVENTOR: Kevin A. Jarrell, Arlington, MA
ASSIGNEE: President and Fellows of Harvard College, Cambridge, MA (U.S. corp.)
APPL-NO: 08/119,512
DATE FILED: Sep. 10, 1993
ART-UNIT: 185
PRIM-EXMR: Mindy Fleisher
ASST-EXMR: Philip W. Carter

LEGAL-REP: Matthew P. Vincent, Giulio A.Lahive & Cockfield DeConti, Jr.

US PAT NO: 5,498,531 [IMAGE AVAILABLE] L3: 10 of 11

ABSTRACT:
The present invention makes available methods and reagents for novel manipulation of nucleic acids. As described herein, the present invention makes use of the ability of intronic sequences, such as derived from group I, group II, or nuclear pre-mRNA introns, to mediate specific cleavage and ligation of discontinuous nucleic acid molecules. For example, novel genes and gene products can be generated by admixing nucleic acid constructs which comprise exon nucleic acid sequences flanked by intron sequences that can direct trans-splicing of the exon sequences to each other. The flanking intronic sequences can, by intermolecular complementation, form a reactive complex which promotes the transesterification reactions necessary to cause the ligation of discontinuous nucleic acid sequences to one another, and thereby generate a recombinant gene comprising the ligated exons.
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FILE 'HOME' ENTERED AT 11:14:27 ON 15 MAY 1997

=> file medline

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY     SESSION
FULL ESTIMATED COST                                         0.15        0.15

FILE 'MEDLINE' ENTERED AT 11:14:41 ON 15 MAY 1997

 FILE LAST UPDATED: 14 MAY 1997 (19970514/UP).  FILE COVERS 1966 TO DATE.
 +QLF/CT SHOWS YOU THE ALLOWABLE QUALIFIERS OF A TERM.

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 AUTHORED OR CO-AUTHORED BY DR. BERNARD FISHER WITH THE PHRASE
 "SCIENTIFIC MISCONDUCT-DATA TO BE REANALYZED."  ALL SUCH ANNOTATIONS
 HAVE BEEN REMOVED OR ARE BEING REMOVED.  WE APOLOGIZE FOR ANY PROBLEMS
 OR CONCERNS THIS MAY HAVE CAUSED.  USERS SHOULD DISREGARD THOSE PRIOR
 ANNOTATIONS.

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 SUBSTANCE IDENTIFICATION.

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E2            1      KHOSITSETH A/AU
E3            0  --> KHOSLA/AU
E4           23      KHOSLA A/AU
E5            1      KHOSLA A A/AU
E6            1      KHOSLA A D/AU
E7            1      KHOSLA A H/AU
E8            1      KHOSLA A K/AU
E9            1      KHOSLA A S/AU
E10           1      KHOSLA B/AU
E11          32      KHOSLA C/AU
E12           5      KHOSLA D/AU

=> s e11

L1           32 "KHOSLA C"/AU
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Phe(P) represents the phosphonic acid analogue of phenylalanine and (O)Phe and (O)Ala represent (L.)-beta-phenyllactic and (L)-lactic acid, respectively. Optically pure peptidyl diazomethyl ketones 16 and 22 were synthesized for selection of the catalytic ensemble of cysteine proteases. An optically pure dipeptidyl boronic acid 26 was synthesized for the selection of the catalytic ensemble of serine proteases. A strategy for the evolution of catalytic antibodies using these haptens was developed which includes mechanism-based selections. Since mechanism based selections result in covalent trapping of ***species*** from ***libraries*** , diol and disulfide containing haptenic linkers were developed for the oxidative or reductive release of selected catalysts.

L19 ANSWER 5 OF 56 MEDLINE
AN 96210089 MEDLINE
TI Pharmacologic characterization of CHIR 2279, an N-substituted glycine peptoid with high-affinity binding for alpha 1-adrenoceptors.
AU Gibbons J A; Hancock A A; Vitt C R; Knepper S; Buckner S A; Brune M E; Milicic I; Kerwin J F Jr; Richter L S; Taylor E W; Spear K L; Zuckermann R N; Spellmeyer D C; Braeckman R A; Moos W H
CS Chiron Corporation, Emeryville, California, USA.
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1996 May) 277 (2) 885-99.
Journal code: JP3. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9608
AB We characterize the in vitro and in vivo pharmacology of CHIR 2279, an N-substituted glycine peptoid previously identified from a ***combinatorial*** ***library*** as a novel ligand to alpha 1-adrenoceptors. Competitive receptor-binding assays with [3H]prazosin showed that CHIR 2279 was similar to prazosin in binding to alpha 1A (rat submaxillary), alpha 1a, alpha 1b, and alpha 1 d (cDNA expressed in LTK- cells) with high and approximately equipotent affinity. Ki values for CHIR 2279 ranged from 0.7 to 3 nM, and were 10-fold weaker than with prazosin. Functional assays for postsynaptic alpha 1-adrenoceptors showed CHIR 2279 was approximately equipotent in antagonizing agonist-induced contractile responses with rat was deferens (alpha 1A), canine prostate (alpha 1A), rat spleen (alpha 1B) and rat aorta (alpha 1D). The pA2 for CHIR 2279 averaged 7.07 in these assays, indicating a 10- to 100-fold lower in vitro potency than prazosin. In dogs, CHIR 2279 antagonized the epinephrine-induced increase in intraurethal pressure (pseudo pA2, 6.86) and in rats antagonized the

phenylephrine-induced increase in mean arterial blood pressure. In rats and guinea pigs, CHIR 2279 induced a dose-dependent decrease in mean arterial blood pressure without eliciting the tachycardia commonly observed with other alpha 1-blockers. Pharmacokinetic/pharmacodynamic modeling showed the i.v. system clearance rate of CHIR 2279 was 60 and 104 ml/min/kg in rats and guinea pigs, respectively, and the in vivo potency for mean arterial blood pressure reduction was twice as great in guinea pigs (EC50, 520 ng/ml) than rats (EC50, 1170 ng/ml).

L19 ANSWER 6 OF 56 MEDLINE
AN 96315620 MEDLINE
TI Oxygen sensing and molecular adaptation to hypoxia.
AU Bunn H F; Poyton R O
CS Division of Hematology/Oncology, Brigham and Women's Hospital, Harvard Medical School, Boston, Masachusetts, USA.
NC GM30228 (NIGMS)
GM39324 (NIGMS)
DK41234 (NIDDK)
SO PHYSIOLOGICAL REVIEWS, (1996 Jul) 76 (3) 839-85. Ref: 388
Journal code: P7M. ISSN: 0031-9333.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 9611
AB This review focuses on the molecular stratagems utilized by bacteria, yeast, and mammals in their adaptation to hypoxia. Among this broad range of organisms, changes in oxygen tension appear to be sensed by heme proteins, with subsequent transfer of electrons along a signal transduction pathway which may depend on reactive oxygen ***species*** . These heme-based sensors are generally two-domain proteins. Some are hemokinases, while others are flavohemoproteins [flavohemoglobins and NAD(P)H oxidases]. Hypoxia-dependent kinase activation of transcription factors in nitrogen-fixing bacteria bears a striking analogy to the phosphorylation of hypoxia inducible factor-1 (HIF-1) in mammalian cells. Moreover, redox chemistry appears to play a critical role both in the trans-activation of oxygen-responsive ***genes*** in unicellular organisms as well as in the activation of HIF-1. In yeast and bacteria, regulatory operons coordinate expression of ***genes*** responsible for adaptive responses to hypoxia and hyperoxia. Similarly, in mammals, ***combinatorial*** interactions of HIF-1 with other identified transcription factors are required for the hypoxic induction of physiologically important

genes .

L19 ANSWER 7 OF 56 MEDLINE DUPLICATE 4
AN 96286052 MEDLINE
TI Determinants of polyreactivity in a large panel of recombinant human antibodies from HIV-1 infection.
AU Ditzel H J; Itoh K; Burton D R
CS Department of Immunology, The Scripps Research Institute, La Jolla, CA 92037, USA.
NC AI33292 (NIAID)
SO JOURNAL OF IMMUNOLOGY, (1996 Jul 15) 157 (2) 739-49.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9701
EW 19970104
AB A considerable part of the Ab repertoire is given over to polyreactive Abs capable of interacting with multiple antigenic ***species*** . Neither the function of these Abs nor the molecular basis for their activity is known. To address the latter problem, we have compared the amino acid sequences of a large panel (n = 70) of polyreactive human monoclonal Fab fragments and conducted a series of engineering experiments on a prototype polyreactive Fab. The Fab fragments were retrieved from ***combinatorial*** IgG ***libraries*** prepared from the bone marrow of long term asymptomatic HIV-1 seropositive donors. The general features displayed by the panel of IgG polyreactive Abs include 1) skewed VH family usage with a predominance of VH1 and VH4 clones and a paucity of the normally prevalent VH3 family; 2) use of a variety of different VH germ-line ***genes*** within the context of the family usage and no restriction in D or JH ***gene*** usage; 3) skewed VL ***gene*** usage: 75% of Fabs used one of two germ lines; and 4) extensive somatic modification of both heavy and light chains. The importance of the heavy chain, in particular the heavy chain CDR3 (HCDR3), in dictating the polyreactive phenotype was demonstrated for the prototype Fab by chain shuffling and CDR transplantation experiments. in addition, and most strikingly, a constrained peptide based on the HCDR3 sequence was shown to be polyreactive and to inhibit binding of the parent Ab to a panel of Ags. A role for conformational flexibility in polyreactivity was suggested by a marked temperature dependence of Ab recognition of Ag. One Ab was shown to be polyreactive at 37 degrees C, but was apparently monoreactive at 4 degrees C. We hypothesize that Ab polyreactivity is associated with conformationally flexible HCDR3 regions in the context of certain favorable framework

configurations.

L19 ANSWER 8 OF 56 MEDLINE DUPLICATE 5
AN 97032597 MEDLINE
TI Classification and phylogeny of the MADS-box multigene family suggest defined roles of MADS-box ***gene*** subfamilies in the morphological evolution of eukaryotes.
AU Theissen G; Kim J T; Saedler H
CS Max-Planck-Institut fur Zuchtungsforschung, Abteilung Molekulare Pflanzengenetik, Carl-von-Linne-Weg 10, D-50829 Koln, Germany.
SO JOURNAL OF MOLECULAR EVOLUTION, (1996 Nov) 43 (5) 484-516. Journal code: J76. ISSN: 0022-2844.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9704
EW 19970404
AB The MADS-box encodes a novel type of DNA-binding domain found so far in a diverse group of transcription factors from yeast, animals, and seed plants. Here, our first aim was to evaluate the primary structure of the MADS-box. Compilation of the 107 currently available MADS-domain sequences resulted in a signature which can strictly discriminate between ***genes*** possessing or lacking a MADS-domain and allowed a classification of MADS-domain proteins into several distinct subfamilies. A comprehensive phylogenetic analysis of known eukaryotic MADS-box ***genes*** , which is the first comprising animal as well as fungal and plant homologs, showed that the vast majority of subfamily members appear on distinct subtrees of phylogenetic trees, suggesting that subfamilies represent monophyletic ***gene*** clades and providing the proposed classification scheme with a sound evolutionary basis. A reconstruction of the history of the MADS-box ***gene*** subfamilies based on the taxonomic distribution of contemporary subfamily members revealed that each subfamily comprises highly conserved putative orthologs and recent paralogs. Some subfamilies must be very old (1,000 MY or more), while others are more recent. In general, subfamily members tend to share highly similar sequences, expression patterns, and related functions. The defined ***species*** distribution, specific function, and strong evolutionary conservation of the members of most subfamilies suggest that the establishment of different subfamilies was followed by rapid fixation and was thus highly advantageous during eukaryotic evolution. These ***gene*** subfamilies may have been essential prerequisites for the establishment of several complex eukaryotic body structures, such as muscles in animals and certain reproductive structures in higher plants, and of some signal transduction

pathways. Phylogenetic trees indicate that after establishment of different subfamilies, additional ***gene*** duplications led to a further increase in the number of MADS-box ***genes*** . However, several molecular mechanisms of MADS-box ***gene*** diversification were used to a quite different extent during animal and plant evolution. Known plant MADS-domain sequences diverged much faster than those of animals, and ***gene*** duplication and sequence diversification were extensively used for the creation of new ***genes*** during plant evolution, resulting in a relatively large number of interacting ***genes*** . In contrast, the available data on animal ***genes*** suggest that increase in ***gene*** number was only moderate in the lineage leading to mammals, but in the case of MEF2-like ***gene*** products, heterodimerization between different splice variants may have increased the ***combinatorial*** possibilities of interactions considerably. These observations demonstrate that in metazoan and plant evolution, increased ***combinatorial*** possibilities of MADS-box ***gene*** product interactions correlated with the evolution of increasingly complex body plans.

L19 ANSWER 9 OF 56 BIOSIS COPYRIGHT 1997 BIOSIS
AN 96:519587 BIOSIS
DN 99241943
TI Discovery of a herbicidal lead using polymer-bound activated esters in generating a ***combinatorial*** ***library*** of amides and esters.
AU Parlow J J; Normansell J E
CS Ceregen Div. Monsanto Co.-U2D, 800 North Lindbergh Blvd., St. Louis, MO 63167, USA
SO Molecular Diversity 1 (4). 1996. 266-269. ISSN: 1381-1991
LA English
AB A ***combinatorial*** ***library*** containing mixtures of amides and esters was prepared through solid-phase chemistry. The advantages of using solid-phase chemistry over solution-phase chemistry to prepare this ***library*** are discussed. The ***library*** was screened through a high-throughput whole organism herbicidal assay upon which a mixture containing amides was found to have herbicidal activity. Deconvolution of the mixture provided N-((3-benzoylphenyl)-3-(1, 1-dimethylethyl)-1-methyl)-1H-pyrazole-5-carboxamide as a herbicidal lead with broadleaf and narrowleaf pre-emergence herbicidal activity as low as 100 g/ha on some weed ***species*** . This study represents the first report of an agrochemical discovered using a ***combinatorial*** approach.

L19 ANSWER 10 OF 56 MEDLINE DUPLICATE 6
AN 96234687 MEDLINE
TI The use of reverse transcription polymerase chain reaction to

analyse large numbers of mRNA ***species*** from a single cell.
AU Toellner K M; Scheel-Toellner D; Seitzer U; Sprenger R; Trumper L; Schluter C; Flad H D; Gerdes J
CS Department of Immunology and Cell Biology, Forschungsinstitut Borstel, Germany.
SO JOURNAL OF IMMUNOLOGICAL METHODS, (1996 May 10) 191 (1) 71-5. Journal code: IFE. ISSN: 0022-1759.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9609
AB A PCR method is described for determining the expression of multiple heterogeneous mRNAs from single cells. The total mRNA pool of a single selected cell is subjected to reverse transcription and subsequent tailing with poly(dA). This cDNA is preamplified by a sequence non-specific PCR protocol using oligo(dT)-containing primers. The single cell cDNA ***library*** obtained permits the analysis of virtually unlimited numbers of mRNA ***species*** per cell using sequence-specific PCR. This procedure of multiple mRNA analysis enables phenotyping of any cell for its mRNA composition and could be used to study the cytokine mRNA expression of individual human T cells ex vivo. The method should greatly facilitate the analysis of ***combinatorial*** expression of known ***genes*** in any cell.

L19 ANSWER 11 OF 56 BIOSIS COPYRIGHT 1997 BIOSIS
AN 97:33306 BIOSIS
DN 99339709
TI Synthesis and screening of a "one-bead-one-compound" ***combinatorial*** peptide ***library*** .
AU Lam K S; Lebl M
CS Arizona Cancer Cent., Dep. Med., Microbiol. Immunology, Coll. Med., Univ. Arizona, 1501 N. Campbell Avenue, Tucson, AZ 85724, USA
SO Methods in Molecular and Cellular Biology 6 (1). 1995-1996. 46-56. ISSN: 0898-7750
LA English
AB By using a "split-synthesis" method in conjunction with standard soiid-phase peptide synthesis, a ***library*** of peptide beads can be synthesized so there is only one unique peptide ***species*** on each bead-the "one-bead-one-compound" concept. With an appropriate screening method targeted for a specific biological, physical, or biochemical property, a unique peptide bead can be identified, physically isolated, and the peptide structure determined. The screening method may involve (1) on-bead assay such as direct binding or covalent modification or (2) releasable assay in which the peptides are released from the bead for biological or

biochemical testing. Examples of these methods for various targets will be described. This one-bead-one-peptide ***library*** method enables one to synthesize and screen 10-7 unique peptides routinely and rapidly and has proved to be an invaluable tool for basic research and drug discovery.

L19 ANSWER 12 OF 56 BIOSIS COPYRIGHT 1997 BIOSIS
AN 96:475169 BIOSIS
DN 99204725
TI Pharmaceutical applications of peptidomimetics.
AU Qabar M; Urban J; Sia C; Klein M; Kahn M
CS Molecumetics Ltd., 2023 120th Ave. N.E., Suite 400, Bellevue, WA 98005, USA
SO Letters in Peptide Science 3 (1). 1996. 25-30. ISSN: 0929-5666
LA English
AB Nature has used a ' ***library*** approach' to constructing ligands for specific receptors and enzymes by combining a limited functional diversity of 20 amino acid side chains with a small array of secondary structure motifs - reverse turns, alpha-helices and beta-strands. The dissection of multidomain proteins into small synthetic conformationally restricted components is an important step in the design of low-molecular-weight nonpeptides that mimic the activity of the native protein. Mimetics of critical functional domains might possess beneficial properties with regard to specificity and therapeutic potential compared to the intact proteinaceous ***species*** . ***Combinatorial*** secondary-structure-templated ***libraries*** provide a powerful engine for the development of novel vaccines and pharmaceuticals.

L19 ANSWER 13 OF 56 MEDLINE DUPLICATE 7
AN 96305135 MEDLINE
TI Dual color microscopic imagery of cells expressing the green fluorescent protein and a red-shifted variant.
AU Yang T T; Kain S R; Kitts P; Kondepudi A; Yang M M; Youvan D C
CS Cell Biology Group, CLONTECH Laboratories, Inc., Palo Alto, CA 94303, USA.
NC GM42645 (NIGMS)
SO GENE, (1996) 173 (1 Spec No) 19-23.
Journal code: FOP. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9611
AB The green fluorescent protein (GFP) from the jellyfish, Aequorea victoria, has become a versatile reporter for monitoring ***gene*** expression and protein localization in a variety of

cells and organisms. GFP emits bright green light (lambda max = 510 nm) when excited with ultraviolet (UV) or blue light (lambda max = 395 nm, minor peak at 470 nm). The chromophore in GFP is intrinsic to the primary structure of the protein, and fluorescence from GFP does not require additional ***gene*** products, substrates or other factors. GFP fluorescence is stable, ***species*** -independent and can be monitored noninvasively using the techniques of fluorescence microscopy and flow cytometry [Chalfie et al., Science 263 (1994) 802-805; Stearns, Curr. Biol. 5 (1995) 262-264]. The protein appears to undergo an autocatalytic reaction to create the fluorophore [Heim et al., Proc. Natl. Acad. Sci. USA 91 (1994) 12501-12504] in a process involving cyclization of a Tyr66 aa residue. Recently [Delagrave et al., Bio/Technology 13 (1995) 151-154], a ***combinatorial*** mutagenic strategy was targeted at aa 64 through 69, which spans the chromophore of A. victoria GFP, yielding a number of different mutants with red-shifted fluorescence excitation spectra. One of these, RSGFP4, retains the characteristic green emission spectra (lambda max = 505 nm), but has a single excitation peak (lambda max = 490 nm). The fluorescence properties of RSGFP4 are similar to those of another naturally occurring GFP from the sea pansy, Renilla reniformis [Ward and Cormier, Photobiochem. Photobiol. 27 (1978) 389-396]. In the present study, we demonstrate by fluorescence microscopy that selective excitation of A. victoria GFP and RSGFP4 allows for spectral separation of each fluorescent signal, and provides the means to image these signals independently in a mixed population of bacteria or mammalian cells.

L19 ANSWER 14 OF 56 MEDLINE
AN 96079012 MEDLINE
TI A mimotope from a solid-phase peptide ***library*** induces a measles virus-neutralizing and protective antibody response.
AU Steward M W; Stanley C M; Obeid O E
CS Department of Clinical Sciences, London School of Hygiene & Tropical Medicine, United Kingdom.
SO JOURNAL OF VIROLOGY, (1995 Dec) 69 (12) 7668-73.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9603
AB A solid-phase 8-mer random ***combinatorial*** peptide ***library*** was used to generate a panel of mimotopes of an epitope recognized by a monoclonal antibody to the F protein of measles virus (MV). An inhibition immunoassay was used to show that these peptides were bound by the monoclonal antibody with different affinities. BALB/c mice were coimmunized with the individual

mimotopes and a T-helper epitope peptide (from MV fusion protein), and the reactivity of the induced anti-mimotope antibodies with the corresponding peptides and with MV was determined. The affinities of the antibodies with the homologous peptides ranged from 8.9 x 10(5) to 4.4 x 10(7) liters/mol. However, only one of the anti-mimotope antibodies cross-reacted with MV in an enzyme-linked immunosorbent assay and inhibited MV plaque formation. Coimmunization of mice with this mimotope and the T-helper epitope peptide induced an antibody response which conferred protection against fatal encephalitis induced following challenge with MV and with the structurally related canine distemper virus. These results indicate that peptide ***libraries*** can be used to identify mimotopes of conformational epitopes and that appropriate immunization with these mimotopes can induce protective antibody responses.

L19 ANSWER 15 OF 56 MEDLINE DUPLICATE 8
AN 96032402 MEDLINE
TI Increased structural and ***combinatorial*** diversity in an extended family of ***genes*** encoding Vlp surface proteins of Mycoplasma hyorhinis.
AU Yogev D; Watson-McKown R; Rosengarten R; Im J; Wise K S
CS Department of Molecular Microbiology and Immunology, School of Medicine, University of Missouri, Columbia 65212, USA.
NC AI 31656 (NIAID)
SO JOURNAL OF BACTERIOLOGY, (1995 Oct) 177 (19) 5636-43.
Journal code: HH3. ISSN: 0021-9193.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U35016
EM 9601
AB Variable lipoproteins (Vlp) constitute the major coat protein of Mycoplasma hyorhinis. They are products of multiple, divergent, single-copy ***genes*** organized in a chromosomal cluster. Three ***genes*** , vlpA, vlpB, and vlpC, have been previously identified in clonal isolates of M. hyorhinis SK76. Each is linked to a characteristic promoter region containing a homopolymeric tract of adenine residues [poly(A) tract], subject to hypermutation, that transcriptionally controls phase variation of vlp ***genes*** and leads to ***combinatorial*** surface mosaics of distinct Vlp products. The size of the natural vlp ***gene*** repertoire is unknown but may critically determine the degree of structural and ***combinatorial*** diversity available in this ***species*** . In this study, the vlp repertoire of M. hyorhinis GDL-1 was characterized and shown to contain three additional ***genes*** , vlpD, vlpE, and vlpF, clustered with other known vlp ***genes***

in the order 5'-vlpD-vlpE-vlpF-IS-vlpA-IS-vlpB-vlpC+ ++-3', where IS represents copies of the IS1221 element of M. hyorhinis. The 5' boundary of this expanded family was identical to that of the more limited family 5'-vlpA-IS-vlpB-vlpC-3' previously described in a clonal isolate of strain SK76. A recombinant construct containing vlpD, vlpE, and vlpF expressed antigenically distinguishable products corresponding to each ***gene*** . These ***genes*** encode characteristic C-terminal repetitive regions that are subject to size variation by insertion or deletion of intragenic repeats but maintain an extended, charged structure. Each vlp ***gene*** also contained characteristic alternative open reading frames, which provide a potential reservoir of coding sequence for Vlp diversity, possibly recruited through insertion and/or deletion mutations.(ABSTRACT TRUNCATED AT 250 WORDS)

L19 ANSWER 16 OF 56 MEDLINE
AN 96422872 MEDLINE
TI Yeast transcriptional regulatory mechanisms.
AU Struhl K
CS Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, Massachusetts 02115, USA.
SO ANNUAL REVIEW OF GENETICS, (1995) 29 651-74. Ref: 151
Journal code: 6DP. ISSN: 0066-4197.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 9702
EW 19970204
AB Transcriptional regulation directly influences many biological phenomena such as cell growth, response to environmental change, development of multicellular organisms, and disease. Transcriptional regulatory mechanisms are fundamentally similar in eukaryotic organisms (93). Components of the basic RNA polymerase II (Pol II) machinery are highly conserved and, in some cases, functionally interchangeable. Transcription factors with similar structures and DNA-binding specificities are found throughout the eukaryotic kingdom, and acidic activation domains stimulate transcription across a wide range of ***species*** . Complex promoters with multiple protein binding sites are typical in all eukaryotic organisms, and efficient transcription generally requires the ***combinatorial*** and synergistic action of activator proteins that function at long and variable distances from the mRNA initiation site. Molecular mechanisms of eukaryotic transcriptional regulation have been elucidated from the studies that involve a wide

variety of ***genes*** , promoters, proteins, organisms, and experimental approaches. This review focuses on transcriptional regulatory mechanisms in the baker's yeast Saccharomyces cerevisiae. Studies in yeast have emphasized powerful genetic approaches that are not available in other eukaryotic organisms. As a consequence, yeast is particularly amenable for analyzing transcriptional regulatory mechanisms in vivo under true physiological conditions. Furthermore, classical and molecular yeast genetics has permitted the discovery and functional characterization of transcriptional regulatory proteins that were not identified in biochemical studies. Thus, genetic analysis in yeast has often generated information complementary to that obtained from biochemical studies of transcription in vitro, and it has provided unique insights into mechanisms of eukaryotic transcriptional regulation.

L19 ANSWER 17 OF 56 MEDLINE DUPLICATE 9
AN 95327049 MEDLINE
TI Genetic analysis of cinnamyl alcohol dehydrogenase in loblolly pine: single ***gene*** inheritance, molecular characterization and evolution.
AU MacKay J J; Liu W; Whetten R; Sederoff R R; O'Malley D M
CS Department of Genetics, North Carolina State University, Raleigh 27695-8008, USA.
SO MOLECULAR AND GENERAL GENETICS, (1995 Jun 10) 247 (5) 537-45. Journal code: NGP. ISSN: 0026-8925.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-Z37991; GENBANK-Z37992
EM 9510
AB The ***gene*** encoding the monolignol biosynthetic enzyme cinnamyl alcohol dehydrogenase (CAD, E.C. 1.1.1.195) can be expressed in response to different developmental and environmental cues. Control of Cad ***gene*** expression could involve either differential regulation of more than one Cad ***gene*** or, alternatively ***combinatorial*** regulation of a single Cad ***gene*** . In loblolly pine (Pinus taeda L.), we found several electrophoretic variants (allozymes) of CAD and a high level of heterozygosity (he = 0.46). Analysis of inheritance patterns of pine CAD allozymes gave segregation ratios that were consistent with Mendelian expectations for a single functional ***gene*** . The identity of the full-length Cad cDNA sequence was confirmed by alignment with peptide sequences obtained from purified active enzyme and by extensive similarity to Cad sequences from other ***species*** . Southern blot analysis of genomic DNA using the Cad cDNA as a hybridization probe gave simple patterns, consistent with

our interpretation that pine Cad is a single-copy ***gene*** . Phylogenetic analysis and evolution rate estimates showed that Cad sequences are diverging less rapidly in the gymnosperms than in the angiosperms. The Cad mRNA was present in both lignifying tissues and a non lignifying tissue (the megagametophyte) of pine. The presence of a single ***gene*** suggests that different regulatory mechanisms for a single Cad ***gene*** , rather than differential regulation of several ***genes*** , can account for its expression in response to different cues.

L19 ANSWER 18 OF 56 MEDLINE DUPLICATE 10
AN 96071024 MEDLINE
TI Multiple APC messenger RNA isoforms encoding exon 15 short open reading frames are expressed in the context of a novel exon 10A-derived sequence.
AU Sulekova Z; Reina-Sanchez J; Ballhausen W G
CS Institute for Human Genetics, The University, Erlangen, Germany.
SO INTERNATIONAL JOURNAL OF CANCER, (1995 Nov 3) 63 (3) 435-41. Journal code: GQU. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-Z49090
EM 9602
AB Intragenic splice mechanisms affecting the coding exons 8 to 15 of the human adenomatous polyposis coli (APC) ***gene*** have been analyzed. Three mechanisms within this ***gene*** area were found to contribute to mRNA heterogeneity: (i) facultative expression of exon 9-encoded sequences; (ii) in-frame insertion of a 54-nucleotide sequence encoded by a novel exon located 1.6 kb down-stream from exon 10, provisionally designated APC exon 10A; (iii) skipping of exon 14, resulting in a novel exon 13/15 connection. Interestingly the latter event provided the mRNA with a novel open reading frame, which was terminated after 19 codons of exon 15-derived sequences. ***Combinatorial*** joining of these segments yielded 7 different transcripts in addition to an mRNA ***species*** resulting from an exon 10/15 connection, as determined by cloning and sequence analysis. RT-PCR expression analyses were carried out to demonstrate that this complexity of splice variants is indeed synthesized in cell lines derived from various tissues. Furthermore, in accordance with our findings at the transcript level, we provide Western blot analyses demonstrating that moderate steady-state levels of genuine APC-specific low m.w. polypeptide chains exist. These APC "light chains", however, are not identical with polypeptide chains, which have been reported to accompany apoptosis and necrosis, since the molecules described here

are definitively co-expressed with p300apc at the transcript and protein levels.

L19 ANSWER 19 OF 56 MEDLINE DUPLICATE 11
AN 95131418 MEDLINE
TI Deconvolution of ***combinatorial*** ***libraries*** for drug discovery: a model system.
AU Freier S M; Konings D A; Wyatt J R; Ecker D J
CS ISIS Pharmaceuticals, Carlsbad, California 92008..
SO JOURNAL OF MEDICINAL CHEMISTRY, (1995 Jan 20) 38 (2) 344-52. Journal code: J0F. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9504
AB Iterative synthesis and screening strategies have recently been used to identify unique active molecules from complex synthetic ***combinatorial*** ***libraries*** . These techniques have many advantages over traditional screening methods, including the potential to screen large numbers of compounds to identify an active molecule while avoiding analytical separations and structural determination of unknown compounds. It is not clear, however, whether these techniques identify the most active molecular ***species*** in the mixtures and, if so, how often. Two key factors which may affect success of the selection process are the presence of many active compounds in the ***library*** with a range of activities and the chosen order of unrandomization. The importance of these factors has not been previously studied. Moreover, the impact of experimental errors in determination of subset activities or in randomization during ***library*** synthesis is not known. We describe here a model system based on oligonucleotide hybridization that addresses these questions using computer simulations. The results suggested that, within achievable experimental and ***library*** synthesis error, iterative deconvolution methods generally find either the best molecule or one with activity very close to the best. The presence of many active compounds in a ***library*** influenced the profile of subset activities, but did not preclude selection of a molecule with near optimal activity.

L19 ANSWER 20 OF 56 BIOSIS COPYRIGHT 1997 BIOSIS
AN 96:27756 BIOSIS
DN 98599891
TI Mating type control of sexual development in Coprinus cinereus.
AU Casselton L A; Asante-Owusu R N; Banham A H; Kingsnorth C S; Kues U; O'Shea S F; Pardo E H

CS Dep. Plant Sci., Univ. Oxford, South Parks Road, Oxford OX1 3RB, UK
SO Canadian Journal of Botany 73 (SUPPL. 1). 1995. S266-S272. ISSN: 0008-4026
LA English
AB The multiallelic mating type ***genes*** of the hymenomycete fungus Coprinus cinereus determine mating compatibility by regulating a developmental sequence that converts an asexual monokaryon into a fertile dikaryon. The ***genes*** map to two loci, A and B, and mating compatibility requires different alleles of ***genes*** at both loci. The A ***genes*** encode two classes of proteins with conserved but dissimilar homeodomain DNA binding motifs (HD1 and HD2), which identify their role in development as transcriptional regulators. Transformation studies with cloned ***genes*** suggest that a compatible mating is sensed by ***combinatorial*** interactions between an HD1 and HD2 protein and that the N-terminal regions of these proteins are implicated in the specificity of this interaction. The B ***genes*** of C. cinereus have been cloned but their function is, as yet, unknown. In another ***species*** , Schizophyllum commune, the B ***genes*** encode pheromones and pheromone receptors. Although a pheromone response pathway is not apparent in cell fusion in hymenomycetes, it now seems likely to be involved in maintenance of dikaryotic growth.

L19 ANSWER 21 OF 56 MEDLINE DUPLICATE 12
AN 95364610 MEDLINE
TI ***Combinatorial*** expression of immediate early ***genes*** in single neurons.
AU Sheng H Z; Lin P X; Nelson P G
CS Laboratory of Developmental Neurobiology, NICHD, NIH, Bethesda, MD 20892, USA.
SO BRAIN RESEARCH. MOLECULAR BRAIN RESEARCH, (1995 Jun) 30 (2) 196-202. Journal code: MBR. ISSN: 0169-328X.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9511
AB To address the question how relatively small numbers of immediate early ***gene*** (IEG) could specifically couple a wide range of stimulus-response cascades, we examined the possibility that IEG could be expressed heterogeneously in individual neurons. Analysis of multiple IEG in single neurons revealed that many individual DRG neurons express several IEGs. The ***combinatorial*** expression of IEGs by individual DRG displays substantial heterogeneity. Analysis of mRNA ***species*** encoding AP-1 composition in single cells also revealed coordinated change of mRNAs coding for AP-1 factors after membrane depolarization. Our results indicate

that differential expression of IEG in individual cells, and the possible interaction among them may represent a mechanism by which the specificity in stimulation-response coupling may be achieved by IEGs.

L19 ANSWER 22 OF 56 MEDLINE DUPLICATE 13
AN 95310841 MEDLINE
TI Generation of immunoglobulin light chain ***gene*** diversity in Raja erinacea is not associated with somatic rearrangement, an exception to a central paradigm of B cell immunity.
AU Anderson M K; Shamblott M J; Litman R T; Litman G W
CS Department of Biochemistry, University of South Florida, All Children's Hospital, St. Petersburg 33701, USA.
NC RO1AI23338 (NIAID)
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1995 Jul 1) 182 (1) 109-19. Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-U19001; GENBANK-U19002; GENBANK-U19003; GENBANK-U19004; GENBANK-U19005; GENBANK-U19006; GENBANK-U19007; GENBANK-U19008; GENBANK-U19009; GENBANK-U19010; GENBANK-U19011; GENBANK-U19012; GENBANK-U19013; GENBANK-U19014; GENBANK-U19015; GENBANK-U19016; GENBANK-U19017; GENBANK-U19018; GENBANK-U19019; GENBANK-U19020; GENBANK-U19021; GENBANK-U19022; GENBANK-U19023; GENBANK-U19024; GENBANK-U19025; GENBANK-U19045; GENBANK-U19046; GENBANK-U19047; GENBANK-U19048; GENBANK-U19049
EM 9509
AB In all vertebrate ***species*** examined to date, rearrangement and somatic modification of ***gene*** segmental elements that encode portions of the antigen-combining sites of immunoglobulins are integral components of the generation of antibody diversity. In the phylogenetically primitive cartilaginous fishes, ***gene*** segments encoding immunoglobulin heavy and light chain loci are arranged in multiple clusters, in which segmental elements are separated by only 300-400 bp. In some cases, segmental elements are joined in the germline of nonlymphoid cells (joined ***genes***). Both genomic ***library*** screening and direct amplification of genomic DNA have been used to characterize at least 89 different type I light chain ***gene*** clusters in the skate, Raja. Analyses of predicted nucleotide sequences and predicted peptide structures are consistent with the distribution of ***genes*** into different sequence groups. Predicted amino acid sequence differences are preferentially distributed in complementarity-determining versus framework regions, and replacement-type substitutions exceed neutral substitutions. When specific germline

sequences are related to the sequences of individual cDNAs, it is apparent that the joined ***genes*** are expressed and are potentially somatically mutated. No evidence was found for the presence of any type I light chain ***gene*** in Raja that is not germline joined. The type I light chain ***gene*** clusters in Raja appear to represent a novel ***gene*** system in which ***combinatorial*** and junctional diversity are absent.

L19 ANSWER 23 OF 56 MEDLINE DUPLICATE 14
AN 95384202 MEDLINE
TI Enhanced quantitative resistance against fungal disease by ***combinatorial*** expression of different barley antifungal proteins in transgenic tobacco.
AU Jach G; Gornhardt B; Mundy J; Logemann J; Pinsdorf E; Leah R; Schell J; Maas C
CS Max-Planck Institut Fur Zuchtungsforschung, Abeteilung Genetische Grundlagen der Pflanzenzuchtung, Cologne, Germany..
SO PLANT JOURNAL, (1995 Jul) 8 (1) 97-109.
Journal code: BRU. ISSN: 0960-7412.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9512
AB cDNAs encoding three proteins from barley (Hordeum vulgare), a class-II chitinase (CHI), a class-II beta-1,3-glucanase (GLU) and a Type-I ribosome-inactivating protein (RIP) were expressed in tobacco plants under the control of the CaMV 35S-promoter. High-level expression of the transferred ***genes*** was detected in the transgenic plants by Northern and Western blot analysis. The leader peptides in CHI and GLU led to accumulation of these proteins in the intercellular space of tobacco leaves. RIP, which is naturally deposited in the cytosol of barley endosperm cells, was expressed either in its original cytosolic form or fused to a plant secretion peptide (spRIP). Fungal infection assays revealed that expression of the individual ***genes*** in each case resulted in an increased protection against the soilborne fungal pathogen Rhizoctonia solani, which infects a range of plant ***species*** including tobacco. To create a situation similar to 'multi- ***gene*** ' tolerance, which traditional breeding experience has shown to provide crops with a longer-lasting protection, several of these antifungal ***genes*** were combined and protection against fungal attack resulting from their co-expression in planta was evaluated. Transgenic tobacco lines were generated with tandemly arranged ***genes*** coding for RIP and CHI as well as GLU and CHI. The performance of tobacco plants co-expressing the barley transgenes GLU/CHI or CHI/RIP in a Rhizoctonia solani infection assay revealed

significantly enhanced protection against fungal attack when compared with the protection levels obtained with corresponding isogenic lines expressing a single barley transgene to a similar level. The data indicate synergistic protective interaction of the co-expressed antifungal proteins in vivo.

L19 ANSWER 24 OF 56 MEDLINE
AN 95249177 MEDLINE
TI Immunotechnological trends in radioimmunotargeting: from 'magic bullet' to 'smart bomb'.
AU Hazra D K; Britton K E; Lahiri V L; Gupta A K; Khanna P; Saran S
CS Postgraduate Department of Medicine, S.N. Medical College, Agra, India..
SO NUCLEAR MEDICINE COMMUNICATIONS, (1995 Feb) 16 (2) 66-75. Ref: 22
Journal code: OB8. ISSN: 0143-3636.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9508
AB The impact of recent advances in the chemical and genetic engineering manipulations of antibodies on radioimmunotargeting is reviewed both in relation to radioimmunoscintigraphy and radioimmunotherapy. The resulting trends are: (1) the linking of parts of the mouse/rat and human antibody molecule; (2) the creation of molecules with dual antigen or multiple antigen recognition capabilities; (3) the making of smaller and smaller antigen recognition molecules; and (4) the development of molecules with dual capabilities, e.g. antigen recognition and enzyme activity. The various methods of creating antibodies in vitro are reviewed with reference to bacteria, using phage selection and a ***combinatorial*** ***library*** , mammalian cells, yeast cells and, finally, mice containing giant yeast artificial chromosomes. The advantages and disadvantages of smaller fragments as well as of the human anti-mouse antibody (HAMA) reaction are discussed and the need for early clinical evaluation and widespread availability of the newer antibodies is emphasized. It is envisaged that these immunotechnological advances will permit the large-scale production of precisely engineered humanized antibodies, and the specificity and affinity rate constant of these antibodies can be optimized using in vitro phage selection as well as by computer modelling where the stereo chemistry of the antigen is known precisely.

L19 ANSWER 25 OF 56 MEDLINE

AN 94308216 MEDLINE
TI Functional analysis of the placenta-specific enhancer of the human glycoprotein hormone alpha subunit ***gene*** . Emergence of a new element.
AU Pittman R H; Clay C M; Farmerie T A; Nilson J H
CS Department of Pharmacology, Case Western Reserve University, School of Medicine, Cleveland, Ohio 44106-4965..
NC DK28559 (NIDDK)
DK43039 (NIDDK)
DK08612 (NIDDK)
+
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Jul 29) 269 (30) 19360-8. Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9410
AB Placental expression of the alpha subunit ***gene*** of the human glycoprotein hormones requires a multicomponent enhancer composed of tandem cAMP-response elements and an adjacent upstream regulatory element. Based on recent studies indicating that the upstream regulatory element includes binding sites for more than one protein, we investigated how functional activity correlated with these binding sites. Through extensive replacement mutagenesis of the native promoter regulatory region, we provide the first functional map of the upstream regulatory element. Within this region, we find that distinct proteins interact with three overlapping binding sites. While each site is functionally significant, no single site is essential or displays clear dominance. This is surprising since one of the sites binds a placenta-specific protein that heretofore has been regarded as essential for activity of the human alpha subunit placenta-specific enhancer. Consequently, our refined functional map of the upstream regulatory element reveals a complex ***combinatorial*** code that directs expression of the human alpha subunit ***gene*** to placenta.

L19 ANSWER 26 OF 56 MEDLINE DUPLICATE 15
AN 94193607 MEDLINE
TI A family of mitogen-activated protein kinase-related proteins interacts in vivo with activator protein-1 transcription factor.
AU Bernstein L R; Ferris D K; Colburn N H; Sobel M E
CS Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892..
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Apr 1) 269 (13) 9401-4. Journal code: HIV. ISSN: 0021-9258.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9407
AB The activator protein-1 (AP-1) transcription factor modulates expression of ***genes*** involved in growth regulation, differentiation, and neoplastic transformation. Several mitogen-activated protein kinases (MAP kinases) as well as other kinases phosphorylate c-Jun and c-Fos in vitro and are postulated to control AP-1 activity. However, since many protein kinases phosphorylate substrates in vitro with which they have no association in vivo, we sought evidence for interaction in vivo between AP-1 and MAP kinase proteins. We now report detection of an association in vivo of MAP kinase-related proteins with c-Jun and AP-1 dimers by peptide mapping and two-dimensional electrophoretic analyses of proteins co-immunoprecipitated with AP-1 antigens. Extracellular signal-regulated kinase-2 and several apparently novel MAP kinase-related proteins are among the ***species*** that bind to AP-1. The large number of MAP kinase-related proteins associated with AP-1 implicates them on an important ***gene*** regulation pathway. ***Combinatorial*** association between MAP kinase-related proteins and AP-1 dimers could potentially create numerous distinct complexes that could regulate diverse ***genes*** .

L19 ANSWER 27 OF 56 MEDLINE DUPLICATE 16
AN 94224811 MEDLINE
TI The nature of the autoimmune antibody repertoire in human immunodeficiency virus type 1 infection.
AU Ditzel H J; Barbas S M; Barbas C F 3rd; Burton D R
CS Department of Immunology, Scripps Research Institute, La Jolla, CA 92037.
NC 1 RO1 AI33292-01 ARRA (NIAID)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Apr 26) 91 (9) 3710-4.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-U07162; GENBANK-U07194; GENBANK-U07195; GENBANK-U07196
EM 9408
AB Human immunodeficiency virus type 1 (HIV-1) seropositive donors typically have high serum antibody titers to a range of autoantigens, and the corresponding autoantibodies have been suggested to be of importance in the pathogenesis of HIV-1

infection. We have prepared 38 IgG human monoclonal autoantibodies from asymptomatic HIV-1 seropositive donors with elevated serum titers to autoantigens by construction of Fab ***combinatorial*** ***libraries*** on the surface of phage and affinity selection using a range of autoantigens, including double-stranded DNA, major histocompatibility complex class II, CD14, epidermal growth factor receptor, and ganglioside GD2. The autoantibodies are shown to be of moderate affinity and exhibit marked cross-reactivity with a range of antigens. This contrasts with the specific high-affinity antibodies selected (i) against infectious agents using the same ***libraries*** and (ii) against one of the autoantigens using a ***library*** from a donor with established autoimmune disease. The results lend no support to the presence of specific autoantibodies in HIV-1 infection and instead suggest attention should be focused on the pathological significance of high serum levels of antibodies capable of interacting with multiple molecular ***species*** .

L19 ANSWER 28 OF 56 MEDLINE DUPLICATE 17
AN 94267510 MEDLINE
TI ***Combinatorial*** expression of three zebrafish ***genes*** related to distal-less: part of a homeobox ***gene*** code for the head.
AU Akimenko M A; Ekker M; Wegner J; Lin W; Westerfield M
CS Loeb Institute for Medical Research, Ottawa, Ontario, Canada..
NC HD 22486 (NICHD)
SO JOURNAL OF NEUROSCIENCE, (1994 Jun) 14 (6) 3475-86.
Journal code: JDF. ISSN: 0270-6474.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U03875; GENBANK-U03876
EM 9409
AB We describe analysis of zebrafish distal-less-related homeobox ***genes*** that may serve as specifiers of positional information in anterior regions of the CNS and in peripheral structures. We isolated three zebrafish ***genes*** , dlx2, dlx3, and dlx4, by screening embryonic cDNA ***libraries*** . Comparisons of the predicted sequences of the Dlx2, Dlx3, and Dlx4 proteins with distal-less proteins from other ***species*** suggest that vertebrate distal-less ***genes*** can be divided into four orthologous groups. We observed similarities but also unique features of the expression patterns of the zebrafish dlx ***genes*** . Among the three ***genes*** , dlx3 alone is expressed during gastrulation. Shortly after gastrulation, cells in the ventral forebrain rudiment express dlx2 and dlx4, but not dlx3,

and hindbrain neural crest cells express only dlx2. Presumptive precursor cells of the olfactory placodes express dlx3 and dlx4 but not dlx2. Transcripts of dlx3 and dlx4 are present in overlapping subsets of cells in the auditory vesicle and in cells of the median fin fold, whereas dlx2 is never expressed in the auditory vesicle and only at low levels in localized regions of the median fin fold. Cells of the visceral arches and their primordia express all three dlx ***genes*** , but with different developmental time courses. We suggest that ***combinatorial*** expression of the dlx ***genes*** is part of a homeobox ***gene*** code specifying pattern formation or cell fate determination in the forebrain, in peripheral structures of the head, and in the fins.

L19 ANSWER 29 OF 56 MEDLINE DUPLICATE 18
AN 94195818 MEDLINE
TI An evolutionarily conserved palindrome in the Drosophila Gld promoter directs tissue-specific expression.
AU Gunaratne P; Ross J L; Zhang Q; Organ E L; Cavener D R
CS Department of Molecular Biology, Vanderbilt University, Nashville, TN 37235..
NC GM34170 (NIGMS)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Mar 29) 91 (7) 2738-42.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9407
AB A conserved palindromic sequence (Gpal) in the promoter region of the Drosophila Gld directs expression of a heterologous reporter ***gene*** in transgenic flies to the anterior spiracular glands of third instar larvae and to the ejaculatory bulb of adult males. The Gld ***gene*** is normally expressed at high levels in the anterior spiracular glands but is not expressed in the ejaculatory bulb of Drosophila melanogaster. However, Gld promoters from other Drosophila ***species*** contain the Gpal element and express glucose dehydrogenase (GLD) in the adult male ejaculatory bulb. A ***gene*** fusion composed of the D. melanogaster Gld promoter and the lacZ ***gene*** is expressed in the anterior spiracular glands of transgenic larvae. Mutations of the Gpal sequence element in this ***gene*** fusion block expression of beta-galactosidase in the anterior spiracular gland. Together these experiments demonstrate that Gpal is necessary and sufficient for tissue-specific expression in the anterior spiracular glands. Based upon the tissue distribution and function of GLD, it is speculated that expression of GLD in the anterior spiracular glands represents

the ancestral state and that GLD expression in other tissues arose as a fortuitous consequence of a shared ***combinatorial*** regulatory network.

L19 ANSWER 30 OF 56 MEDLINE DUPLICATE 19
AN 95154823 MEDLINE
TI ***Gene*** structure prediction by linguistic methods.
AU Dong S; Searls D B
CS Department of Genetics, University of Pennsylvania School of Medicine, Philadelphia 19104..
SO GENOMICS, (1994 Oct) 23 (3) 540-51.
Journal code: GEN. ISSN: 0888-7543.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9505
AB The higher-order structure of ***genes*** and other features of biological sequences can be described by means of formal grammars. These grammars can then be used by general-purpose parsers to detect and to assemble such structures by means of syntactic pattern recognition. We describe a grammar and parser for eukaryotic protein-encoding ***genes*** , which by some measures is as effective as current connectionist and ***combinatorial*** algorithms in predicting ***gene*** structures for sequence database entries. Parameters of the grammar rules are optimized for several different ***species*** , and mixing experiments are performed to determine the degree of ***species*** specificity and the relative importance of compositional, signal-based, and syntactic components in ***gene*** prediction.

L19 ANSWER 31 OF 56 MEDLINE
AN 94182913 MEDLINE
TI Engineering and production of streptokinase in a Bacillus subtilis expression-secretion system.
AU Wong S L; Ye R; Nathoo S
CS Department of Biological Sciences, University of Calgary, Alberta, Canada..
SO APPLIED AND ENVIRONMENTAL MICROBIOLOGY, (1994 Feb) 60 (2) 517-23.
Journal code: 6K6. ISSN: 0099-2240.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9406
AB Streptokinase is one of the major blood-clot-dissolving agents used in many medical treatments. With the cloned streptokinase

gene (skc) available, production of the secreted streptokinase from various Bacillus subtilis strains was studied. The use of the six-extracellular-protease-deficient strain, WB600, greatly improved the production yield of the secreted streptokinase. A modified skc which has the original skc promoter and signal sequence replaced with the B. subtilis levansucrase promoter and signal sequence was also constructed. B. subtilis carrying either the wild-type or the modified skc produces streptokinase at a comparable level. Even with WB600 as the expression host, a C-terminally-processed streptokinase was also observed. Through region-specific ***combinatorial*** mutagenesis around the C-terminal processing sites, streptokinase derivatives resistant to C-terminal degradation were engineered. One of the derivatives showed a 2.5-fold increase in specific activity and would potentially be a better thrombolytic agent.

L19 ANSWER 32 OF 56 MEDLINE DUPLICATE 20
AN 95211277 MEDLINE
TI The Cladophora complex (Chlorophyta): new views based on 18S rRNA ***gene*** sequences.
AU Bakker F T; Olsen J L; Stam W T; van den Hoek C
CS Department of Marine Biology, University of Groningen, Haren, The Netherlands..
SO MOLECULAR PHYLOGENETICS AND EVOLUTION, (1994 Dec) 3 (4) 365-82. Journal code: BYP. ISSN: 1055-7903.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-Z35313; GENBANK-Z35314; GENBANK-Z35315; GENBANK-Z35316; GENBANK-Z35317; GENBANK-Z35318; GENBANK-Z35319; GENBANK-Z35320; GENBANK-Z35321; GENBANK-Z35322; GENBANK-Z35323; GENBANK-Z35324; GENBANK-Z35417; GENBANK-Z35418; GENBANK-Z35419; GENBANK-Z35420; GENBANK-Z35421; GENBANK-Z35422; GENBANK-Z35423; GENBANK-Z35424
EM 9507
AB Evolutionary relationships among ***species*** traditionally ascribed to the Siphonocladales/Cladophorales have remained unclear due to a lack of phylogenetically informative characters and extensive morphological plasticity resulting in morphological convergence. This study explores some of the diversity within the generic complex Cladophora and its siphonocladalaen allies. Twelve ***species*** of Cladophora representing 6 of the 11 morphological sections recognized by van den Hoek were analyzed along with 8 siphonocladalaen ***species*** using 18S rRNA ***gene*** sequences. The final alignment consisted of 1460 positions containing 92 phylogenetically informative substitutions. Weighting schemes (EOR weighting, ***combinatorial*** weighting) were

applied in maximum parsimony analysis to correct for substitution bias. Stem characters were weighted 0.66 relative to single-stranded characters to correct for secondary structural constraints. Both weighting approaches resulted in greater phylogenetic resolution. Results confirm that there is no basis for the independent recognition of the Cladophorales and Siphonocladales. The Siphonocladales is polyphyletic, and Cladophora is paraphyletic. All analyses support two principal lineages, of which one contains predominantly tropical members including almost all siphonocladalean taxa, while the other lineage consists of mostly warm- to cold-temperate ***species*** of Cladophora.

L19 ANSWER 33 OF 56 MEDLINE DUPLICATE 21
AN 93345601 MEDLINE
TI Diversity of expressed V and J regions of immunoglobulin light chains in Xenopus laevis.
AU Stewart S E; Du Pasquier L; Steiner L A
CS Department of Biology, Massachusetts Institute of Technology, Cambridge 02139..
NC AI-08054 (NIAID)
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (1993 Aug) 23 (8) 1980-6. Journal code: EN5. ISSN: 0014-2980.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-15570; GENBANK-15571; GENBANK-15572; GENBANK-15573; GENBANK-15574; GENBANK-15575; GENBANK-15576; GENBANK-15577; GENBANK-15578; GENBANK-15579; GENBANK-15580; GENBANK-15581; GENBANK-15582; GENBANK-15583; GENBANK-15584; GENBANK-15585; GENBANK-15586; GENBANK-15587; GENBANK-15588; GENBANK-15589; GENBANK-15590; GENBANK-15591; GENBANK-15592; GENBANK-L15570; GENBANK-L15571; GENBANK-L15572; GENBANK-L15573; GENBANK-L15574; GENBANK-L15575; GENBANK-L15576; +
EM 9311
AB In Xenopus laevis, two immunoglobulin light chain isotypes, designated L1 or rho and L2 or sigma, have been identified. The genomic organization of the L1 locus has been described previously: a constant (C) ***gene*** segment is preceded by a joining (J) ***gene*** segment; in addition, there are many cross-hybridizing variable (V) ***gene*** segments. To evaluate the extent of sequence diversity of L1 V regions, we screened three cDNA ***libraries*** , constructed from mitogen-stimulated Xenopus splenocytes, with probes for the C or the J ***gene*** segment. Eighteen cDNA clones that contain complete or truncated V regions were chosen for sequence analysis. The C regions of all clones are identical or nearly identical to the genomic C ***gene***

segment; the V regions are greater than 80% identical in nucleotide sequence and are presumably derived from a single family of V ***gene*** segments. Although framework regions are nearly identical, complementarity-determining regions are quite diverse. The expressed J segments fall into distinct groups, suggesting the presence of more than one germ-line J segment. Therefore, a genomic ***library*** was screened with a J region probe. A clone overlapping with the previously identified J-C clone, and containing four additional J ***gene*** segments, was isolated. All five J ***gene*** segments are very similar and three are identical in nucleotide sequence. Each of the three distinct germ-line J sequences is represented in the set of cDNA clones, suggesting that ***combinatorial*** diversification occurs; imprecision of V-J joining also appears to contribute to variability. Overall, these results suggest that the immunoglobulin repertoire in this ***species*** is not significantly restricted by a limitation in the diversity of light chain V regions.

L19 ANSWER 34 OF 56 MEDLINE DUPLICATE 22
AN 93353137 MEDLINE
TI Somatic variation precedes extensive diversification of germline sequences and ***combinatorial*** joining in the evolution of immunoglobulin heavy chain diversity.
AU Hinds-Frey K R; Nishikata H; Litman R T; Litman G W
CS Department of Pediatrics, University of South Florida, All Children's Hospital, St. Petersburg, Florida 33701..
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1993 Sep 1) 178 (3) 815-24. Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-Z11776; GENBANK-Z11777; GENBANK-Z11778; GENBANK-Z11779; GENBANK-Z11780; GENBANK-Z11781; GENBANK-Z11782; GENBANK-Z11783; GENBANK-Z11784; GENBANK-Z11785; GENBANK-Z11786; GENBANK-Z11787; GENBANK-Z11788; GENBANK-Z11790; GENBANK-Z11791; GENBANK-Z11792
EM 9311
AB In Heterodontus, a phylogenetically primitive shark ***species*** , the variable (VH), diversity (DH), joining (JH) segments, and constant (CH) exons are organized in individual approximately 18-20-kb "clusters." A single large VH family with > 90% nucleic acid homology and a monotypic second ***gene*** family are identified by extensive screening of a genomic DNA ***library*** . Little variation in the nucleotide sequences of DH segments from different germline ***gene*** clusters is evident, suggesting that the early role for DH was in promoting junctional diversity rather than contributing unique coding specificities. A ***gene***

-specific oligodeoxynucleotide screening method was used to relate specific transcription products (cDNAs) to individual ***gene*** clusters and showed that ***gene*** rearrangements are intra- rather than intercluster. This provides further evidence for restricted diversity in the immunoglobulin heavy chain of Heterodontus, from which it is inferred that ***combinatorial*** diversity is a more recently acquired means for generating diversity. The observed differences between cDNA sequences selected and the sequences of segmental elements derived from conventional genomic ***libraries*** as well as from VH segment-specific ***libraries*** generated by direct PCR amplification of genomic DNA indicate that the VH repertoire is diversified by both junctional diversity and somatic mutation. Taken together, these findings suggest a heretofore unrecognized contribution of somatic variation that preceded both extensive diversification of the germline repertoire and the ***combinatorial*** joining process in the evolution of humoral immunity.

L19 ANSWER 35 OF 56 BIOSIS COPYRIGHT 1997 BIOSIS
AN 93:274514 BIOSIS
DN BA96:4739
TI ***GENE*** REGULATION OF FLOWERING.
AU BRADLEY D; CARPENTER R; ELLIOTT R; SIMON R; ROMERO J; HANTKE S; DOYLE S; MOONEY M; LUO D; ET AL
CS DEP. GENETICS, AFRC INST. PLANT SCI. RES., JOHN INNES CENTRE, COLONEY LANE, NORWICH NR4 7UH, UK.
SO PHILOS TRANS R SOC LOND B BIOL SCI 339 (1288). 1993. 193-197. CODEN: PTRBAE ISSN: 0080-4622
LA English
AB A major change in the development of plants occurs upon floral induction. Meristems in certain positions become organized to form flowers. We are studying this process using a combination of genetic, molecular and physiological approaches in Antirrhinum. In particular, we are exploiting transposon-induced mutations in ***genes*** controlling early switches in floral development. These mutations cause homeotic and heterochronic phenotypes and three categories of ***genes*** have been identified. The first includes floricaula (flo), which is required to switch inflorescence meristems to a floral state. This ***gene*** has been isolated and shown to be expressed transiently in bract, sepal, petal and carpel primordia. The second group of ***genes*** controls the identity (and sometimes the number) of organs in a whorl. These ***genes*** affect overlapping whorls and their mutant phenotypes suggest a ***combinatorial*** model for ***gene*** action in determining the fate of floral primordia. Some of the regulatory interactions between these ***genes*** have been revealed by studying cis- or trans-acting mutations which have resulted in ectopic ***gene***

expression. ***Genes*** of the third category determine the identity of organs within one whorl and thus affect the symmetry of the flower. We propose that the interactions of these homeotic ***genes*** control the basic patterns of inflorescence and flower development not only in Antirrhinum, but also in a diverse range of plant ***species*** .

L19 ANSWER 36 OF 56 MEDLINE
AN 93367340 MEDLINE
TI ***Combinatorial*** ***libraries*** .
AU Persson M A
CS Karolinska Institute, Department of Medicine, Karolinska Hospital, Stockholm, Sweden..
SO INTERNATIONAL REVIEWS OF IMMUNOLOGY, (1993) 10 (2-3) 153-63. Ref: 42
Journal code: IRI. ISSN: 0883-0185.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9312
AB ***Combinatorial*** antibody ***libraries*** , in which PCR amplified immunoglobulin light and heavy chain DNA are randomly recombined irrespective of their pairing in vivo into a vector and subsequently expressed in E. coli, have quickly become a very productive tool to generate monoclonal antibodies from various ***species*** . It has been drastically improved by utilizing phage display technologies in the selection process of specific antibodies. A brief summary of current techniques, critical published experiments showing the versatility of these systems with emphasis on human antibodies and discussions on chain preference, affinity maturation and the advent of semisynthetic and non-immune ***libraries*** will be presented.

L19 ANSWER 37 OF 56 MEDLINE
AN 93099842 MEDLINE
TI GLOBOSA: a homeotic ***gene*** which interacts with DEFICIENS in the control of Antirrhinum floral organogenesis.
AU Trobner W; Ramirez L; Motte P; Hue I; Huijser P; Lonnig W E; Saedler H; Sommer H; Schwarz-Sommer Z
CS Max-Planck-Institut fur Zuchtungsforschung, Koln, Germany.
SO EMBO JOURNAL, (1992 Dec) 11 (13) 4693-704.
Journal code: EMB. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
OS GENBANK-M94779; GENBANK-M94780; GENBANK-M94781; GENBANK-M94782; GENBANK-M94783; GENBANK-M94784; GENBANK-M94785; GENBANK-X67816; GENBANK-X67817; GENBANK-X68831
EM 9303
AB GLOBOSA (GLO) is a homeotic ***gene*** whose mutants show sepaloid petals and carpelloid stamens. The similarity of Glo mutants to those of the DEFICIENS (DEFA) ***gene*** suggests that the two ***genes*** have comparable functions in floral morphogenesis. The GLO cDNA has been cloned by virtue of its homology to the MADS-box, a conserved DNA-binding domain also contained in the DEFA ***gene*** . We have determined the structure of the wild type GLO ***gene*** as well as of several glo mutant alleles which contain transposable element insertions responsible for somatic and germinal instability of Glo mutants. Analyses of the temporal and spatial expression patterns of the DEFA and GLO ***genes*** during development of wild type flowers and in flowers of various stable and unstable defA and glo alleles indicate independent induction of DEFA and GLO transcription. In contrast, organ-specific up-regulation of the two ***genes*** in petals and stamens depends on expression of both DEFA and GLO. In vitro DNA-binding studies were used to demonstrate that the DEFA and GLO proteins specifically bind, as a heterodimer, to motifs in the promoters of both ***genes*** . A model is presented which proposes both ***combinatorial*** and cross-regulatory interactions between the DEFA and GLO ***genes*** during petal and stamen organogenesis in the second and third whorls of the flower. The function of the two ***genes*** controlling determinate growth of the floral meristem is also discussed.

L19 ANSWER 38 OF 56 MEDLINE
AN 93046712 MEDLINE
TI Protein engineering of antibodies.
AU Sandhu J S
CS Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Ontario, Canada..
SO CRITICAL REVIEWS IN BIOTECHNOLOGY, (1992) 12 (5-6) 437-62. Ref: 182
Journal code: CRB. ISSN: 0738-8551.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9302
AB This article reviews the technical advances in antibody engineering

and the clinical applications of these molecules. Recombinant DNA technology facilitates the construction and expression of engineered antibodies. These novel molecules are designed to meet specific applications. Although genomic and cDNA cloning have been used widely in the past to isolate the relevant antibody V domains, at present, the PCR-based cloning is the preferred system. Bacterial and mammalian expression systems are used commonly for the production of antibodies, antibody fragments, and antibody fusion proteins. A range of chimeric antibodies with murine V domains joined to C regions from human and other ***species*** have been produced and found to exhibit the expected binding characteristics and effector functions. Humanized antibodies have been developed to minimize the HAMA response, and bifunctional immunoglobulins are being used in tumor therapy and diagnosis. Single chain antibodies and fusion proteins with antibody specificities jointed to nonimmunoglobulin sequences provide a source of antibody-like molecules with novel properties. The potential applications of minimal recognition units and antigenized antibodies are described. ***Combinatorial*** ***libraries*** produced in bacteriophage present an alternative to hybridomas for the production of antibodies with the desired antigen binding specificities. Future developments in this field are discussed also.

L19 ANSWER 39 OF 56 MEDLINE DUPLICATE 23
AN 92355112 MEDLINE
TI T-cell receptor gamma/delta: comparison of ***gene*** configurations and function between humans and chimpanzees.
AU Sturm E; Bontrop R E; Vreugdenhil R J; Otting N; Bolhuis R L
CS Department of Immunology, Dr. Daniel den Hoed Cancer Center, Rotterdam, The Netherlands..
SO IMMUNOGENETICS, (1992) 36 (5) 294-301.
Journal code: GI4. ISSN: 0093-7711.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-X61069; GENBANK-M73960; GENBANK-M83073; GENBANK-M83074; GENBANK-M83075; GENBANK-M83077; GENBANK-M81095; GENBANK-M81096; GENBANK-M81097; GENBANK-M81098
EM 9211
AB The human and chimpanzee T-cell receptor gamma-delta (TCR gamma delta) bearing cells represent a minor subset (3-8%) of T lymphocytes. In the periphery, the TCR gamma delta population has a restricted ***combinatorial*** repertoire. The TCRD-V1 and -V2 ***gene*** products are expressed in a mutually exclusive fashion, whereas, the TCRD-V2 and the TCRG-V9 encoded proteins show, in general, a coordinated expression. Restriction fragment length

polymorphism analysis showed conservation of the restriction sites that identify the TCRG-V9 and TCRD-V2 rearrangements. The human TCRG-V9 locus has two alleles, TCRG-V9A1 and TCRG-V9A2 differing at codon position 31. The chimpanzee TCRG-V9 ***gene*** product differs from the products of the human TCRG-V9A1 and TCRG-V9A2 allele by two and three amino acid replacements, respectively. The human and the chimpanzee TCRG-V9-TCRD-V2 lymphocytes show a similar specific proliferative and cytolytic response to human Daudi Burkitt's lymphoma cells. Therefore, the amino acid replacements found in the chimpanzee TCRG-V9 ***gene*** product do not change the superantigen specificity across this ***species*** barrier.

L19 ANSWER 40 OF 56 MEDLINE
AN 92273143 MEDLINE
TI In vitro antibodies: strategies for production and application.
AU Morrison S L
CS Department of Microbiology and Molecular Genetics, University of California, Los Angeles 90024-1489..
NC CA 16858 (NCI)
AI29470 (NIAID)
SO ANNUAL REVIEW OF IMMUNOLOGY, (1992) 10 239-65. Ref: 142
Journal code: ALO. ISSN: 0732-0582.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 9209
AB The approaches to the production of antibodies (Ab) using the techniques of genetic engineering and expression are reviewed. Genetic engineering facilitates the production of proteins tailormade for an intended use. Bacterial and mammalian expression systems are commonly used for the production of Ab and Ab-like molecules. While genomic or cDNA cloning can be used to obtain the relevant variable regions, PCR-based cloning approaches facilitate the acquisition of additional binding specificities. Large numbers of different chimeric Abs with murine variable regions joined to constant regions from human and other ***species*** have been expressed and found to exhibit the expected binding specificities and effector functions. These molecules have been used to study the structural basis of effector functions such as complement activation and Fc receptor binding, and potentially they may be used as therapeutic agents. Carbohydrate has been shown to influence both variable and constant region function. Single-chain Abs and fusion proteins with Ab binding specificities joined to nonimmunoglobulin sequences provide a source of Ab-like molecules with novel

properties, and genetically engineered Ab-like molecules provide a source of useful antigens. ***Combinatorial*** ***libraries*** produced in bacteriophage present an alternative to hybridomas for the production of Abs with desired combining specificities. Issues of the immunogenicity of the recombinant molecules are addressed.

L19 ANSWER 41 OF 56 BIOSIS COPYRIGHT 1997 BIOSIS
AN 92:231572 BIOSIS
DN BA93:119597
TI HUMAN TYPE XIII COLLAGEN CDNA-DERIVED PRIMARY STRUCTURE ALTERNATIVE SPLICING OF PRE-MRNA AND TISSUE DISTRIBUTION OF MRNAS.
AU JUVONEN M
CS COLLAGEN RES. UNIT, BIOCENTER, UNIV. OULU, SF-90220 OULU, FINLAND.
SO ACTA UNIV OULUENSIS SER A SCI RERUM NAT 0 (230). 1992. 5-92. CODEN: AUOADB ISSN: 0355-3191
LA English
AB The complete primary structure of a human collagen encoded by several overlapping cDNAs isolated from an endothelial cell ***library*** was determined. The deduced translation product of the cDNAs was different in structure from that of the other collagen types characterized to date, and the polypeptide encoded by the clones was designated as the .alpha.1(XIII) collagen chain. The deduced polypeptide consists of a putative signal peptide, three collagenous domains, COL1-COL3, and four non-collagenous domains, NC1-NC4, two of them separating the collagenous domains and two located at the N and C-terminal ends of the polypeptide. The human .alpha.1(XIII) collagen ***gene*** is at least 140,000 base pairs (bp) in size and codes for a mRNA of 2500-2800 nucleotides. Type XIII collagen pre-mRNA was shown to be subjected to alternative splicing in a region of nine exons which affects the structure of the outer thirds of the predicted polypeptide, leaving the NC1, COL2 and NC3 domains constant. Amplification of a region, covering the COL1 and NC2 domains demonstrated that at least 12 mRNA ***species*** occur through the alternative use of exons 3B-5, 12 and 13, and as a result the predicted length of the COL1 domain may vary between 57 and 104 amino acid residues, while that of the NC2 domain is either 12, 31 or 34 residues. Characterization of the ***combinatorial*** splicing of exons 29, 33 and 37, which code for parts of the COL3 and NC4 domains, showed five of the eight potential mRNA variants, thus coding for polypeptides with a COL3 domain of 190, 208, 220, 223 or 235 amino acid residues and a NC4 domain of 7 or 18 residues. Furthermore, in the course of this work a previously unidentified -Gly-Xaa-Yaa-encoding exon (4B) was found. No strict tissue or cell-specificity was observed in the pattern of alternative splicing affecting the COL1 and NC2 domains, although distinct differences in the proportions of the mRNA variants were found. The extent of inclusion of exon 12 and 13 sequences in particular varied according

to the type of tissue or cell analysed. Interestingly, the four samples studied more closely appeared to contain only 1-3 major combinations of exons 3B-5, 12 and 13, representing about 50% to nearly 100% of all variants. The topographic distribution of the .alpha.1(XIII) collagen chain was described in several human foetal tissues and the early human placenta by in situ hybridization using either cDNA or RNA probes, and the pattern in the foetal tissues was compared with that of fibrillar collagen types I, II and III. An intense in situ hybridization signal was obtained with the type XIII collagen cDNAs in foetal skin (epidermis, hair follicles and nail root cells), intestine (mucosal layer), bone (fibrous mesenchyme), striated muscle (endomycium) and cartilage. Furthermore, expression of type XIII mRNAs was found in placental villi (fibroblastoid stromal cells, endothelial cells and cells of the cytotrophoblastic columns) and in decidua (large decidual cells of the decidual membrane and stromal cells of the gestational endometrium).

L19 ANSWER 42 OF 56 MEDLINE
AN 92011496 MEDLINE
TI Heterologous cooperativity in Escherichia coli. The CytR repressor both contacts DNA and the cAMP receptor protein when binding to the deoP2 promoter.
AU Pedersen H; Sogaard-Andersen L; Holst B; Valentin-Hansen P
CS Department of Molecular Biology, Odense University, Denmark..
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 Sep 25) 266 (27) 17804-8. Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9201
AB Promoters in Escherichia coli that are negatively regulated by the CytR repressor are also activated by the cAMP receptor protein (CRP) complexed to cAMP; as a characteristic, these promoters encode two binding sites for the cAMP.CRP complex. Biochemical and genetic studies have shown that CytR relies on interactions with the cAMP.CRP complex in order to bind promoter DNA and repress transcription. Here we have purified CytR to near homogeneity and addressed the question of how it interacts with the deoP2 promoter. Gel retardation and DNase I footprinting analyses show that CytR is a true sequence-specific DNA-binding protein that binds to the sequence between the two CRP sites in deoP2 with a relatively low affinity. In the presence of the cAMP.CRP complex the two protein ***species*** bind cooperatively to deoP2, forming a complex in which CytR occupies the sequence between the two DNA bound cAMP.CRP complexes. Furthermore, the inducer (cytidine) does not affect independent DNA binding of CytR, rather the CytR/cAMP.CRP

cooperativity is perturbed. These results indicate that CytR binding to deoP2 relies on both repressor-DNA interactions and protein-protein interactions to cAMP.CRP. This ***combinatorial*** repression mechanism, in which an activator functions as an adaptor for a repressor that is not capable of blocking transcription on its own, is unprecedented in prokaryotes; it is, however, reminiscent of repression mechanisms found in eukaryotes.

L19 ANSWER 43 OF 56 MEDLINE DUPLICATE 24
AN 91217092 MEDLINE
TI ***Combinatorial*** mutagenesis of the reactive site region in plasminogen activator inhibitor I.
AU York J D; Li P; Gardell S J
CS Department of Biological Chemistry, Merck Sharp & Dohme Research Laboratories, West Point, Pennsylvania 19486..
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 May 5) 266 (13) 8495-500. Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9108
AB Plasminogen activator inhibitor (PAI-I) rapidly inactivates tissue plasminogen activator (t-PA) and urokinase (UK) with nearly identical association rate constants. The contributions of Ser344, Ala345, and Arg346 (P3, P2, and P1 residues, respectively) in PAI-I to inhibition of UK and t-PA were evaluated using ***combinatorial*** mutagenesis of the human PAI-I cDNA. A bacteriophage lambda expression ***library*** potentially encoding the 8000 unique PAI-I ***species*** were screened for inhibitory activity against UK using a fibrin indicator gel. 390 plaques demarcated by zones of retarded fibrinolysis were analyzed to determine the DNA sequences of their associated active PAI-1 ***species*** . We found 134 unique PAI-1 variants that retained inhibitory activity towards UK; they contained a variety of amino acids in their P3 and P2 positions but only Arg or, infrequently, Lys in their P1 position. Each of the unique active PAI-1 were assayed for inhibitory activity towards UK or t-PA; many substitutions differentially affected the ability of the inhibitor to inactivate UK and t-PA. For example, replacement of Ser344 and Ala344 with Val and Pro, respectively, yielded a PAI-1 variant exhibiting an association rate constant that was unchanged for t-PA but decreased 23-fold for UK, relative to native PAI-1. In general, the PAI-1 variants were more potent inhibitors of t-PA than UK. Hence, t-PA appears more tolerant than UK of structural diversity present in the P3 and P2 positions of the PAI-1 variants.

L19 ANSWER 44 OF 56 MEDLINE
AN 91217063 MEDLINE
TI Tissue- and development-specific alternative RNA splicing regulates expression of multiple isoforms of erythroid membrane protein 4.1.
AU Conboy J G; Chan J Y; Chasis J A; Kan Y W; Mohandas N
CS Cell and Molecular Biology Division, Lawrence Berkeley Laboratory, University of California, Berkeley 94720.
NC DK 32094 (NIDDK)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 May 5) 266 (13) 8273-80. Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-M61733; GENBANK-M77693; GENBANK-M60257; GENBANK-M60258; GENBANK-M60259; GENBANK-M62780; GENBANK-M60203; GENBANK-M60204; GENBANK-M60205; GENBANK-M60206
EM 9108
AB Protein 4.1, a multifunctional structural protein originally described as an 80-kDa component of the erythroid membrane skeleton, exhibits tissue- and development-specific heterogeneity in molecular weight, subcellular localization, and primary amino acid sequence. Earlier reports suggested that some of this impressive heterogeneity is generated by alternative RNA splicing (Conboy, J. G., Chan, J., Mohandas, N., and Kan, Y. W. (1988) Proc. Natl. Acad. Sci. U. S. A. 85, 9062-9065; Tang, T. K., Leto, T., Marchesi, V. T., and Benz, E. J. (1990) J. Cell Biol. 110, 617-624). We have now completed a systematic analysis of 4.1 mRNA isoforms expressed in erythroid cells, and have generated an "alternative splicing map" which summarizes diagrammatically a multitude of polypeptide isoforms potentially generated by ***combinatorial*** splicing of nine alternative exons. Complex 5' splicing events yield mRNA isoforms that may initiate translation at different sites and thus generate elongated or truncated NH2 termini; elongated approximately 135-kDa and prototypical approximately 80-kDa ***species*** were detected in both erythrocytes and T-lymphocytes, but in very different ratios. Among the functional domains of 4.1 responsible for interaction with other membrane skeletal elements, four variants of the 10-kDa spectrin-actin-binding region and four variants of the putative 30-kDa glycophorin-binding region are predicted. Developmentally controlled alternative RNA splicing in the spectrin-actin-binding region may help regulate remodeling of membrane architecture and mechanical properties that occur during erythropoiesis.

L19 ANSWER 45 OF 56 BIOSIS COPYRIGHT 1997 BIOSIS
AN 92:28299 BIOSIS

DN BA93:17574
TI EVOLUTION OF THE IMMUNE SYSTEM THE ORIGIN OF ANTIBODY DIVERSITY.
AU DU PASQUIER L
CS BASEL INST. IMMUNOL., 487 GRENZACHERSTRASSE, CH-4058 BALE, SUISSE.
SO M-S (MED SCI) 7 (7). 1991. 665-673. CODEN: MSMSE4
LA French
AB The immune system of vertebrates started to develop very early in evolution, about 600 million years ago when appeared in primitive fish most of the ***genes*** and cells specific to this system. The solutions chosen during phylogeny in order to generate antibody and T cell receptor repertoires represent variations on a theme, calling in a variable manner ***combinatorial*** rearrangement of genetic elements, ***gene*** conversion and somatic mutations and hypermutations. The selected systems reflect more a good adaptation to features characteristic of the cellular dynamics of the immune system than the filiation relationships between the ***species*** : duration of the period during which the repertoire is produced, number of lymphocytes available, possibility of wastage, mitotic activity of cells, etc.

L19 ANSWER 46 OF 56 MEDLINE DUPLICATE 25
AN 91045896 MEDLINE
TI Evolutionary conservation of antigen recognition: the chicken T-cell receptor beta chain.
AU Tjoelker L W; Carlson L M; Lee K; Lahti J; McCormack W T; Leiden J M; Chen C L; Cooper M D; Thompson C B
CS Howard Hughes Medical Institute, University of Michigan Medical Center, Ann Arbor 48109..
NC CA16673 (NCI)
CA13148 (NCI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1990 Oct) 87 (20) 7856-60.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-M37798; GENBANK-M37799; GENBANK-M37800; GENBANK-M37801; GENBANK-M37802; GENBANK-M37803; GENBANK-M37804; GENBANK-M37805; GENBANK-M37806
EM 9102
AB T cells play important regulatory roles in the immune responses of vertebrates. Antigen-specific T-cell activation involves T-cell receptor (TCR) recognition of a peptide antigen presented by a major histocompatibility complex molecule, and much has been learned about this antigen-recognition process through structural and genetic studies of mammalian TCRs. Although previous studies have

demonstrated that avian T cells express cell-surface molecules analogous to the mammalian TCR heterodimers, TCR ***genes*** have not been identified in nonmammalian ***species*** . We now report the cloning of a cDNA that encodes the beta chain of the chicken TCR. Southern blot analysis using this TCR beta cDNA probe demonstrated that the chicken TCR beta locus was clonally rear-ranged in chicken T-cell lines. TCR beta mRNA was expressed in cells isolated from the thymus but not in cells from the bursa of Fabricius where B cells are generated. Sequence analysis of six additional TCR beta cDNAs suggested the existence of at least two variable (V) region families, three joining (J) elements, and single diversity (D) and constant (C) elements. As in mammals, considerable nucleotide diversity was observed at the junctions of the variable, diversity, and joining elements in chicken TCR beta cDNAs. Genomic V beta and J beta elements were also cloned and sequenced. Both elements are flanked by classical heptamer/nonamer recombination signal sequences. Although the chicken and mammalian TCR beta chains displayed only 31% overall amino acid sequence identity, a number of conserved structural features were observed. These data indicate that (i) the chicken TCR beta repertoire is generated by ***combinatorial*** and junctional diversity and (ii) despite divergent evolution at the level of nucleotide sequence, important structural features of the TCR beta polypeptide are conserved between avian and mammalian ***species*** .

L19 ANSWER 47 OF 56 MEDLINE DUPLICATE 26
AN 90349634 MEDLINE
TI Influenza virus hemagglutinin-specific antibodies isolated from a ***combinatorial*** expression ***library*** are closely related to the immune response of the donor [published erratum appears in Proc Natl Acad Sci U S A 1991 Feb 15;88(4):1590].
AU Caton A J; Koprowski H
CS Wistar Institute of Anatomy and Biology, Philadelphia, PA 19104.
NC AI24541 (NIAID)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1990 Aug) 87 (16) 6450-4.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-M55999; GENBANK-M56000; GENBANK-M56001; GENBANK-M57272; GENBANK-M57273; GENBANK-M57280; GENBANK-M61220; GENBANK-M61226; GENBANK-M61227; GENBANK-M61228
EM 9011
AB Antibodies specific for the influenza virus hemagglutinin have been isolated from a ***combinatorial*** expression ***library***

generated using mRNA obtained from an immunized donor mouse. Sequence analysis indicates that the antibody heavy chain variable regions were derived from members of an expanded hemagglutinin-specific B-cell clone, in conjunction with one of two light chain variable regions. Moreover, the most frequently identified heavy chain variable/light chain variable combination is extremely similar to a heavy chain variable/light chain variable combination that has previously been identified among hemagglutinin-specific hybridoma antibodies. The results, therefore, demonstrate that these antibodies bear a close relationship to the immune status of the donor mouse and suggest that simple adaptations of this procedure might allow evaluation of the immune responses of ***species*** , such as man, in which conventional hybridoma techniques have to date proven ineffective.

L19 ANSWER 48 OF 56 MEDLINE DUPLICATE 27
AN 90349571 MEDLINE
TI Preferential utilization of conserved immunoglobulin heavy chain variable ***gene*** segments during human fetal life.
AU Schroeder H W Jr; Wang J Y
CS Department of Medicine, University of Alabama, Birmingham 35294.
NC AI23694 (NIAID)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1990 Aug) 87 (16) 6146-50.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-M34020; GENBANK-M34021; GENBANK-M34022; GENBANK-M34023; GENBANK-M34024; GENBANK-M34025; GENBANK-M34026; GENBANK-M34027; GENBANK-M34028; GENBANK-M34029; GENBANK-M34030; GENBANK-M34031; GENBANK-M34032
EM 9011
AB The ability to respond to specific antigens develops in a programmed fashion. Although the antibody repertoire in adults is presumably generated by stochastic ***combinatorial*** joining of rearranged heavy variable, diversity, and joining (VH-DH-JH) and light (VL-JL) chains, experimental evidence in the mouse has shown nonrandom utilization of variable ***gene*** segments during ontogeny and in response to specific antigens. In this study, we have performed sequence analysis of 104-day human fetal liver-derived, randomly isolated constant region C+ mu transcripts and demonstrate a consistent preference during fetal life for a small subset of three highly conserved VH3 family ***gene*** segments. In addition, the data show that this preferential ***gene*** segment utilization extends to the DHQ52 and the JH3

and JH4 loci. Sequence analysis of two "sterile" DH-JH transcripts suggests that transcriptional activation of the JH-proximal DHQ52 element may precede initiation of DH-JH rearrangement and influence fetal DH utilization. Sequence comparisons reveal striking nucleotide polymorphism in allelic ***gene*** segments which is poorly reflected in the peptide sequence, implying considerable evolutionary selection pressure. Although vertebrate ***species*** utilize a variety of strategies to generate their antibody repertoire, preferential utilization of VH3 elements is consistently found during early development. These data support the hypothesis that VH3 ***gene*** segments play an essential role in the development of the immune response.

L19 ANSWER 49 OF 56 MEDLINE DUPLICATE 28
AN 90046727 MEDLINE
TI Evolution of immunoglobulin ***genes*** : VH families in the amphibian Xenopus.
AU Hsu E; Schwager J; Alt F W
CS Howard Hughes Medical Institute, New York, NY 10032.
NC AI-20047 (NIAID)
CA-40427 (NCI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1989 Oct) 86 (20) 8010-4.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-M30024; GENBANK-M30025; GENBANK-M30026; GENBANK-M30027; GENBANK-M30028; GENBANK-M30029; GENBANK-M30030; GENBANK-M30031; GENBANK-M30032; GENBANK-M30033; GENBANK-M30034; GENBANK-M30035; GENBANK-M30036; GENBANK-M30037
EM 9002
AB We have isolated multiple independent cDNA clones that represent mRNA sequences of immunoglobulin heavy chains from the spleen of adult Xenopus laevis. These cDNA clones contained constant (C) region sequences that were either Cmu or a separate C region sequence believed to be Cnu. In individual cDNA clones the C region sequences were associated with independent heavy-chain variable region (VH) sequences that were classifiable into five distinct families. Genomic Southern blotting analyses with family-specific probes indicated that the haploid genome contains a minimum of 80 VH ***gene*** segments, a number similar to that found in various mammalian ***species*** . Multiple JH and putative DH segments were also identified (J, joining; D, diversity). Analyses of 13 independent VHDJH junctions suggest that ***combinatorial*** and junctional diversification mechanisms probably arose early in

vertebrate evolution. Finally, comparison of Xenopus VH sequences to those from other vertebrates indicated conservation of V region framework residues that are responsible for the tertiary structure of the Fv throughout evolution.

L19 ANSWER 50 OF 56 MEDLINE
AN 91207931 MEDLINE
TI Evolutionary comparison of the avian IgL locus: ***combinatorial*** diversity plays a role in the generation of the antibody repertoire in some avian ***species*** .
AU McCormack W T; Carlson L M; Tjoelker L W; Thompson C B
CS Howard Hughes Medical Institute, Department of Internal Medicine, University of Michigan Medical School, Ann Arbor 48109.
NC CA48023 (NCI)
SO INTERNATIONAL IMMUNOLOGY, (1989) 1 (4) 332-41.
Journal code: AY5. ISSN: 0953-8178.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-M25720; GENBANK-M25721; GENBANK-M25722; GENBANK-M25723; GENBANK-M25724; GENBANK-M25725; GENBANK-M25726
EM 9108
AB Immunoglobulin light chain (IgL) diversity is generated in the chicken by recombination between the single functional variable (VL) and joining (JL) ***gene*** segments and subsequent somatic diversification of the rearranged VL region. In order to determine whether these events are a general feature of avian IgL ***genes*** , we analyzed the organization and recombinatorial characteristics of the IgL loci of several other avian ***species*** . Southern blot analysis of bursal and germline DNA using chicken VL and constant (CL) probes revealed that the IgL loci of quail, mallard duck, pigeon, turkey, cormorant, and hawk consist of a family of VL elements, but undergo a single major rearrangement event similar to that observed in chickens. In contrast, several rearrangements were observed in the Muscovy duck locus. A phage clone containing a 26 kb insert that hybridized to VL and CL probes was isolated from a Muscovy duck erythrocyte DNA genomic ***library*** . Nucleotide sequencing revealed that the clone contained a single JL-CL region flanked on the 5' side by five VL segments. Unlike the chicken, two of the VL segments (VL1, VL5) appear to be functional. The remaining three VL segments are pseudogenes that lack promoter and leader sequences, but one of these (psi VL3) has recombination signal sequences. Overall, these data indicate that rearrangement of one VL ***gene*** segment is a general feature of the IgL locus in many avian ***species*** . In these ***species*** , the presence of a family of VL elements

that do not rearrange suggests that a pseudogene pool may be available for somatic diversification by ***gene*** conversion. The organization of the Muscovy duck IgL locus suggests that additional combinatiorial diversity has evolved independently in some avian ***species*** .

L19 ANSWER 51 OF 56 MEDLINE
AN 86175072 MEDLINE
TI Major reorganization of immunoglobulin VH segmental elements during vertebrate evolution.
AU Hinds K R; Litman G W
NC AI 23338 (NIAID)
GM 36483 (NIGMS)
SO NATURE, (1986 Apr 10-16) 320 (6062) 546-9.
Journal code: NSC. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-X03750; GENBANK-X03749; GENBANK-X03748
EM 8607
AB In mammals, the immunoglobulin heavy-chain variable region (VH) locus is organized in a linear fashion; individual VH, diversity (DH), joining (JH) and constant (CH) region segments are linked in separate regions. During somatic development, coding segments flanked by characteristic short recombination signal sequences, separated by intervening sequence regions that may exceed 2,000 kilobases (kb), are recombined. ***Combinatorial*** joining of different segments as well as imprecision in this process contribute to the diversity of the primary antibody response; subsequent mutation further alters functionally rearranged ***genes*** . This basic somatic reorganization mechanism is shared by six major families of ***genes*** encoding antigen receptors. Previously, we have shown that multiple germline ***genes*** and mammalian-like recombination signal sequences are associated with the VH ***gene*** family of Heterodontus francisci (horned shark), a primitive elasmobranch. Studies presented here demonstrate that segmental reorganization involving mammalian-like DH and JH segments occurs in the lymphoid tissues of this ***species*** . In marked contrast to the mammalian system, we find multiple instances of close linkage (approximately 10 kb) between individual VH, DH, JH, and CH segments. This unique organization may limit ***combinatorial*** joining and be a factor in the restricted antibody response of this lower vertebrate.

L19 ANSWER 52 OF 56 MEDLINE
AN 84295616 MEDLINE

TI - Immunoglobulin kappa light-chain diversity in rabbit is based on the 3' length heterogeneity of germ-line variable ***genes*** .
AU - Heidmann O; Rougeon F
SO NATURE, (1984 Sep 6-11) 311 (5981) 74-6.
Journal code: NSC. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-X00977; GENBANK-K02438; GENBANK-K02439; GENBANK-K02440
EM 8412
AB Antibody diversity is generated by the ***combinatorial*** association of multiple distinct genetic segments (variable (V), joining (J) and diversity (D) light (L) and heavy (H) chains--VL, JL and VH, D, JH) and amplified somatically by three or four different mechanisms. The kappa system in mouse and human consists of 50-100 V kappa segments associated with a cluster of four or five functional J kappa segments, located 2.5 kilobases (kb) 5' to a single C kappa ***gene*** . The third hypervariable region (CDR3), which is part of the antibody combining site, is usually nine amino acids long in human and mouse kappa chains. It is encoded by the last seven codons of the V kappa segment and the first two of the J kappa segment, one codon sometimes being added or deleted between V and J by junctional variation. In the rabbit, the C kappa 1 ***gene*** which encodes the major isotype, is associated with a cluster of five J kappa segments, only one of which seems to be functional, thus significantly decreasing the ***combinatorial*** potential. However, amino acid sequence comparison has revealed extensive heterogeneity in the length of rabbit CDR3 , suggesting the existence of a D segment analogous to that in the heavy-chain system. We show here that rabbit V kappa ***genes*** have several additional nucleotides at their 3' ends. Thus, even with a single functional J kappa segment, high CDR3 diversity can be generated based on the length heterogeneity of V kappa germ-line segments and their greater length, which might leave scope for an increased junctional deletion.

L19 ANSWER 53 OF 56 BIOSIS COPYRIGHT 1997 BIOSIS
AN 83:191916 BIOSIS
DN BA75:41916
TI THE T LYMPHOCYTE RESPONSE TO CYTOCHROME C 3. RELATIONSHIP OF THE FINE SPECIFICITY OF ANTIGEN RECOGNITION TO MAJOR HISTO COMPATIBILITY COMPLEX GENOTYPE.
AU MATIS L A; HEDRICK S M; HANNUM C; ULTEE M E; LEBWOHL D; MARGOLIASH E; SOLINGER A M; LERNER E A; SCHWARTZ R H
CS LAB. IMMUNOL., NATL. INST. ALLERGY INFECT. DIS., NATL. INST. HEALTH, BETHESDA, MD. 20205, USA.

SO J IMMUNOL 128 (6). 1982. 2439-2446. CODEN: JOIMA3 ISSN: 0022-1767
LA English
AB The fine specificity and genetic control of the murine T lymphocyte proliferative response to the globular protein antigen pigeon cytochrome c was assessed in the high responder strain, B10.S(9R) (H-2t4), and was compared to previously reported results for the B10.A (H-21e) strain. The proliferative response of T cells from both strains was shown to be controlled by 2 complementing major histocompatibility complex- (MHC) linked immune response (IR) ***genes*** and required the presence of the 2 high responder IR alleles in a single antigen-presenting cell. The proliferative responses of T cells from both strains were inhibited by a monoclonal anti-Ia antibody (Y-17) reactive with a common ***combinatorial*** or conformational determinant on the Aes:E.alpha.k (B10.S(9R)) and Aek:E.alpha.k (B10.A) Ia molecules. Evidently the T cells from B10S(9R) and B10.A mice respond to pigeon cytochrome c in the context of homologous Ia molecules that are presumably encoded for by the complementing Ir ***genes*** . The antigenic determinant on pigeon cytochrome c recognized by the B10.S(9R) T cells was the same C-terminal site recognized by the B10.A. Certain fine specificity differences in the responses of the 2 strains could be demonstrated. Whereas B10.A T cells were stimulated by ***species*** variant cytochromes c possessing either the immunodominant glutamine (or serine) at position 100 or the C-terminal lysine at position 103 or 104, B10.S(9R) T cells were generally stimulated only by cytochrome c bearing both of these amino acid residues. Because the 2 strains appeared to recognize similar antigenic determinants in the context of homologous Ia molecules, attempts were made to present pigeon cytochrome c to T cells of 1 strain on antigen-presenting cells from the other. Using pigeon cytochrome c-specific, long-term T cell lines to reduce alloreactivity and magnify the specific response, up to 20% cross-presentation between the 2 strains could be demonstrated. Thus MHC restriction is not absolute, although the degree of degeneracy for even closely homologous Ia molecules is limited.

L19 ANSWER 54 OF 56 MEDLINE
AN 82233690 MEDLINE
TI A family of ***genes*** that codes for ELH, a neuropeptide eliciting a stereotyped pattern of behavior in Aplysia.
AU Scheller R H; Jackson J F; McAllister L B; Schwartz J H; Kandel E R; Axel R
SO CELL, (1982 Apr) 28 (4) 707-19.
Journal code: CQ4. ISSN: 0092-8674.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

OS GENBANK-J01019
EM 8211
AB We describe a particularly advantageous experimental system for studying ***gene*** structure, expression and modulation in the nervous system. In the marine mollusc Aplysia, the bag cells, two discrete clusters of neurons, secrete a peptide of known behavioral function. This neuroactive peptide, egg-laying hormone (ELH), produces a characteristic and stereotypic behavioral repertoire, consisting first of a cessation of walking and inhibition of feeding, followed by head waving and egg laying. We have cloned the ***genes*** encoding ELH and characterized their organization and expression. At least five distinct ***genes*** for ELH exist within the chromosome. Sequence analysis of one recombinant clone unambiguously identifies a contiguous stretch of nucleotides that encodes the 36 amino acids of ELH. Transcription of this small multigene family results in the expression of at least five distinct RNA transcripts encoding ELH. The pattern of transcripts differs strikingly in different tissues: bag cells express three distinct mRNA ***species*** , whereas the atrial gland, a secretory reproductive gland, expresses two distinct mRNAs. Several other neuronal and nonneuronal tissues do not express ELH RNA. In vitro these mRNAs produce a series of long polypeptide precursors that must be processed to generate the active ELH peptide. This processing event is likely to generate several additional neuroactive peptides. Thus the same peptide, ELH, may be released in association with different combinations of other neuroactive peptides. The concept of ***combinatorial*** sets of neuropeptides, each bearing one overlapping peptide ELH, and each directing a differing pattern of behavior, greatly expands the information potential of a small set of ***genes*** .

L19 ANSWER 55 OF 56 BIOSIS COPYRIGHT 1997 BIOSIS
AN 82:295782 BIOSIS
DN BA74:68262
TI A FAMILY OF ***GENES*** THAT CODES FOR EGG LAYING HORMONE A NEURO PEPTIDE ELICITING A STEREOTYPED PATTERN OF BEHAVIOR IN APLYSIA.
AU SCHELLER R H; JACKSON J F; MCALLISTER L B; SCHWARTZ J H; KANDEL E R; AXEL R
CS INST. OF CANCER RESEARCH, COLUMBIA UNIV., COLL. OF PHYSICIANS AND SURGEONS, N.Y., N.Y. 10032.
SO CELL 23 (4). 1982. 707-720. CODEN: CELLB5 ISSN: 0092-8674
LA English
AB A particularly advantageous experimental system for studying ***gene*** structure, expression and modulation in the nervous system is described. In the marine mollusk Aplysia, the bag cells, 2 discrete clusters of neurons, secrete a peptide of known behavioral function. This neuroactive peptide, egg-laying hormone (ELH),

produces a characteristic and stereotypic behavioral repertoire, consisting 1st of a cessation of walking and inhibition of feeding, followed by head waving and egg laying. The ***genes*** encoding ELH were cloned and their organization and expression were characterized. At least 5 distinct ***genes*** for ELH exist within the chromosome. Sequence analysis of 1 recombinant clone unambiguously identifies a contiguous stretch of nucleotides and encodes the 36 amino acids of ELH. Transcription of this small multigene family results in the expression of at least 5 distinct RNA transcripts encoding ELH. The pattern of transcripts differs strikingly in different tissues: bag cells express 3 distinct mRNA ***species*** , whereas the atrial gland, a secretory reproductive gland, expresses 2 distinct mRNA. Several other neuronal and nonneuronal tissues do not express ELH RNA. In vitro these mRNA produce a series of long polypeptide precursors that must be processed to generate the active ELH peptide. This processing event is likely to generate several additional neuroactive peptides. The same peptide, ELH may be released in association with different combinations of other neuroactive peptides. The concept of ***combinatorial*** sets of neuropeptides, each bearing one overlapping peptide ELH, and each directing a differing pattern of behavior, greatly expands the information potential of a small set of ***genes*** .

L19 ANSWER 56 OF 56 MEDLINE
AN 78219250 MEDLINE
TI Light chain diversity of murine anti-streptococcal antibodies: IgCH-linked effects on L chain expression.
AU Perlmutter R M; Briles D E; Greve J M; Davie J M
SO JOURNAL OF IMMUNOLOGY, (1978 Jul) 121 (1) 149-58.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 7811
AB L chains derived from anti-group A streptococcal carbohydrate antibodies raised in A/J, BALB/cJ, C57BL/6J, CB-20, BAB-14, and CAL-20 mice were examined by isoelectric focusing. Multiple strain-associated differences in the degree and frequency of expression of particular L chain spectrotypes were observed. Analysis of L chain-focusing patterns in allotype-congenic mice revealed that IgCH-linked ***genes*** can have profound effects on the L chain phenotypes expressed by strains with identical L chain genotypes. Lastly, the overall spectrotypic diversity of L chains from anti-GAC antibodies appears to be less extensive than the diversity of the antibodies from which these L chains derive,

[redacted]cumented by similar techniques. These results are interpreted in [redacted]ight of the significance of ***combinatorial*** diversity in generating antibody heterogeneity.

=> LOGOFF Y

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